



## Clinical trial results:

### A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of Faricimab in Patients with Neovascular Age-Related Macular Degeneration (LUCERNE)

#### Summary

|                          |                            |
|--------------------------|----------------------------|
| EudraCT number           | 2018-004042-42             |
| Trial protocol           | AT PT DE HU DK ES PL BG IT |
| Global end of trial date | 07 January 2022            |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 01 January 2023 |
| First version publication date | 01 January 2023 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | GR40844 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03823300 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | F. Hoffmann-La Roche, Ltd.  |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland,  |
| Public contact               | F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com |
| Scientific contact           | F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.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                       | 07 January 2022 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 05 October 2020 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 07 January 2022 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy and safety of faricimab compared with aflibercept in patients with neovascular age-related macular degeneration.

Protection of trial subjects:

This study was conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual. All participants were required to read and sign an informed consent form prior to participation in the study.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 11 March 2019 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 66          |
| Country: Number of subjects enrolled | Australia: 38          |
| Country: Number of subjects enrolled | Austria: 14            |
| Country: Number of subjects enrolled | Brazil: 8              |
| Country: Number of subjects enrolled | Bulgaria: 8            |
| Country: Number of subjects enrolled | Denmark: 7             |
| Country: Number of subjects enrolled | France: 26             |
| Country: Number of subjects enrolled | Germany: 6             |
| Country: Number of subjects enrolled | Hong Kong: 9           |
| Country: Number of subjects enrolled | Hungary: 33            |
| Country: Number of subjects enrolled | Italy: 12              |
| Country: Number of subjects enrolled | Korea, Republic of: 35 |
| Country: Number of subjects enrolled | Poland: 46             |
| Country: Number of subjects enrolled | Portugal: 9            |
| Country: Number of subjects enrolled | Russian Federation: 16 |
| Country: Number of subjects enrolled | Singapore: 5           |
| Country: Number of subjects enrolled | Spain: 22              |
| Country: Number of subjects enrolled | Taiwan: 19             |
| Country: Number of subjects enrolled | Turkey: 12             |

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 267 |
| Worldwide total number of subjects   | 658                |
| EEA total number of subjects         | 183                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                      | 63  |
| From 65 to 84 years                       | 492 |
| 85 years and over                         | 103 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 1012 patients were screened, 354 of whom failed screening, most commonly due to not meeting inclusion criteria. A total of 658 treatment-naïve patients with nAMD were randomized 1:1 into the study: 331 to the faricimab arm and 327 to the aflibercept arm.

### Period 1

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

### Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Arm A: Faricimab |

Arm description:

Subjects randomized to Arm A received 6 mg of faricimab intravitreally (IVT) once every 4 weeks (Q4W) up to Week 12 (4 injections). At Week 20, protocol-defined assessment of disease activity required Arm A subjects with active disease to be treated with a once every 8 weeks (Q8W) dosing regimen of 6 mg of faricimab (i.e., at Weeks 20, 28, 36, 44, 52, and 60). A second assessment of disease activity at Week 24 required Arm A subjects with active disease (excluding those with active disease at Week 20) to be treated with a once every 12 weeks (Q12W) dosing regimen of 6 mg of faricimab IVT (i.e., at Weeks 24, 36, 48, and 60). Subjects who did not have active disease at Weeks 20 and 24 were treated with 6 mg of faricimab IVT once every 16 weeks (Q16W; i.e., at Weeks 28, 44, and 60). From Week 60 (when all of Arm A was scheduled to receive study drug) to Week 108, Arm A subjects were to be treated according to a personalized treatment interval (PTI) dosing regimen (Q8W, Q12W, or Q16W).

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Faricimab   |
| Investigational medicinal product code | RO6867461   |
| Other name                             | Vabysmo™, VA2, Humanized anti-VEGF-A anti-Ang-2 bispecific Antibody |
| Pharmaceutical forms                   | Solution for injection  |
| Routes of administration               | Intravitreal use  |

Dosage and administration details:

Subjects randomized to Arm A received 6 mg of faricimab intravitreally (IVT) once every 4 weeks (Q4W) up to Week 12 (4 injections). At Week 20, protocol-defined assessment of disease activity required Arm A subjects with active disease to be treated with a once every 8 weeks (Q8W) dosing regimen of 6 mg of faricimab (i.e., at Weeks 20, 28, 36, 44, 52, and 60). A second assessment of disease activity at Week 24 required Arm A subjects with active disease (excluding those with active disease at Week 20) to be treated with a once every 12 weeks (Q12W) dosing regimen of 6 mg of faricimab IVT (i.e., at Weeks 24, 36, 48, and 60). Subjects who did not have active disease at Weeks 20 and 24 were treated with 6 mg of faricimab IVT once every 16 weeks (Q16W; i.e., at Weeks 28, 44, and 60). From Week 60 (when all of Arm A was scheduled to receive study drug) to Week 108, Arm A subjects were to be treated according to a personalized treatment interval (PTI) dosing regimen (Q8W, Q12W, or Q16W).

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Arm B: Aflibercept |
|------------------|--------------------|

Arm description:

Subjects randomized to the active comparator (Arm B) received a 2-mg dose of aflibercept that was administered intravitreally (IVT) Q8W, after 3 consecutive monthly doses during the 108-week treatment period. Subjects were to receive 15 IVT injections of aflibercept during the 108-week treatment period comprising three initiating injections (2 mg of aflibercept Q4W to Week 8), followed by 12 maintenance injections (2 mg of aflibercept Q8W at Weeks 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, and 104).

|          |                   |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Aflibercept            |
| Investigational medicinal product code |                        |
| Other name                             | Eylea                  |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravitreal use       |

Dosage and administration details:

Subjects randomized to the active comparator (Arm B) received a 2-mg dose of aflibercept that was administered intravitreally (IVT) Q8W, after 3 consecutive monthly doses during the 108-week treatment period. Subjects were to receive 15 IVT injections of aflibercept during the 108-week treatment period comprising three initiating injections (2 mg of aflibercept Q4W to Week 8), followed by 12 maintenance injections (2 mg of aflibercept Q8W at Weeks 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, and 104).

| <b>Number of subjects in period 1</b>    | Arm A: Faricimab | Arm B: Aflibercept |
|--|------------------|--------------------|
| Started                                  | 331              | 327                |
| Received at Least One Dose of Study Drug | 331              | 326                |
| Completed up to Week 48                  | 321              | 309                |
| Completed                                | 297              | 273                |
| Not completed                            | 34               | 54                 |
| Consent withdrawn by subject             | 16               | 22                 |
| Physician decision                       | 1                | 7                  |
| Adverse event, non-fatal                 | 3                | 5                  |
| Death                                    | 10               | 14                 |
| Not Specified                            | 1                | -                  |
| Not Eligible                             | -                | 1                  |
| Lost to follow-up                        | 1                | 3                  |
| Protocol deviation                       | 1                | 1                  |
| Lack of efficacy                         | 1                | 1                  |

## Baseline characteristics

### Reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | Arm A: Faricimab   |
| Reporting group description:   |                    |
| Subjects randomized to Arm A received 6 mg of faricimab intravitreally (IVT) once every 4 weeks (Q4W) up to Week 12 (4 injections). At Week 20, protocol-defined assessment of disease activity required Arm A subjects with active disease to be treated with a once every 8 weeks (Q8W) dosing regimen of 6 mg of faricimab (i.e., at Weeks 20, 28, 36, 44, 52, and 60). A second assessment of disease activity at Week 24 required Arm A subjects with active disease (excluding those with active disease at Week 20) to be treated with a once every 12 weeks (Q12W) dosing regimen of 6 mg of faricimab IVT (i.e., at Weeks 24, 36, 48, and 60). Subjects who did not have active disease at Weeks 20 and 24 were treated with 6 mg of faricimab IVT once every 16 weeks (Q16W; i.e., at Weeks 28, 44, and 60). From Week 60 (when all of Arm A was scheduled to receive study drug) to Week 108, Arm A subjects were to be treated according to a personalized treatment interval (PTI) dosing regimen (Q8W, Q12W, or Q16W). |                    |
| Reporting group title  | Arm B: Aflibercept |
| Reporting group description:   |                    |
| Subjects randomized to the active comparator (Arm B) received a 2-mg dose of aflibercept that was administered intravitreally (IVT) Q8W, after 3 consecutive monthly doses during the 108-week treatment period. Subjects were to receive 15 IVT injections of aflibercept during the 108-week treatment period comprising three initiating injections (2 mg of aflibercept Q4W to Week 8), followed by 12 maintenance injections (2 mg of aflibercept Q8W at Weeks 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, and 104).  |                    |

| Reporting group values                             | Arm A: Faricimab | Arm B: Aflibercept | Total |
|--|------------------|--------------------|-------|
| Number of subjects                                 | 331              | 327                | 658   |
| Age categorical                                    |                  |                    |       |
| Units: Subjects                                    |                  |                    |       |
| In utero   | 0                | 0                  | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                | 0                  | 0     |
| Newborns (0-27 days)                               | 0                | 0                  | 0     |
| Infants and toddlers (28 days-23 months)           | 0                | 0                  | 0     |
| Children (2-11 years)                              | 0                | 0                  | 0     |
| Adolescents (12-17 years)                          | 0                | 0                  | 0     |
| Adults (18-64 years)                               | 30               | 33                 | 63    |
| From 65-84 years                                   | 257              | 235                | 492   |
| 85 years and over                                  | 44               | 59                 | 103   |
| Age Continuous                                     |                  |                    |       |
| Units: Years                                       |                  |                    |       |
| arithmetic mean                                    | 74.8             | 76.1               |       |
| standard deviation                                 | ± 8.4            | ± 8.6              | -     |
| Sex: Female, Male                                  |                  |                    |       |
| Units: Participants                                |                  |                    |       |
| Female   | 203              | 188                | 391   |
| Male   | 128              | 139                | 267   |
| Race/Ethnicity, Customized                         |                  |                    |       |
| Units: Subjects                                    |                  |                    |       |
| White  | 278              | 270                | 548   |
| Asian  | 38               | 34                 | 72    |
| Unknown  | 12               | 17                 | 29    |
| Black or African American                          | 2                | 5                  | 7     |

|  |        |        |        |
|--|--------|--------|--------|
| American Indian or Alaska Native<br>Multiple   | 1<br>0 | 0<br>1 | 1<br>1 |
| Ethnicity (NIH/OMB)<br>Units: Subjects   |        |        |        |
| Hispanic or Latino   | 35     | 46     | 81     |
| Not Hispanic or Latino   | 287    | 274    | 561    |
| Unknown or Not Reported  | 9      | 7      | 16     |
| Region of Enrollment<br>Units: Subjects  |        |        |        |
| United States and Canada   | 135    | 132    | 267    |
| Asia   | 35     | 33     | 68     |
| Rest of the World  | 161    | 162    | 323    |
| Number of Participants by the Eye<br>(Right or Left) Chosen as the Study Eye<br>Units: Subjects  |        |        |        |
| Right Eye  | 168    | 170    | 338    |
| Left Eye   | 163    | 157    | 320    |
| Number of Participants by the BCVA<br>Letter Score Categories in the Study Eye<br>Units: Subjects  |        |        |        |
| ≥74 Letters  | 45     | 39     | 84     |
| 73 to 55 Letters   | 181    | 183    | 364    |
| ≤54 Letters  | 105    | 105    | 210    |
| Number of Participants by the Low<br>Luminance Deficit (LLD) Letter Score<br>Categories in the Study Eye<br>Units: Subjects  |        |        |        |
| <33 Letters  | 238    | 234    | 472    |
| ≥33 Letters  | 89     | 93     | 182    |
| Missing/Invalid  | 4      | 0      | 4      |
| Choroidal Neovascularization (CNV)<br>Lesion Type in the Study Eye by Fundus<br>Fluorescein Angiography<br>Units: Subjects   |        |        |        |
| Occult   | 171    | 140    | 311    |
| Classic  | 98     | 109    | 207    |
| Minimally Classic  | 30     | 31     | 61     |
| Retinal Angiomatous Proliferation<br>(RAP)   | 14     | 15     | 29     |
| Predominantly Classic  | 6      | 16     | 22     |
| Polypoidal Choroidal Vasculopathy<br>(PCV)   | 5      | 8      | 13     |
| Missing  | 7      | 8      | 15     |
| Best Corrected Visual Acuity (BCVA)<br>Letter Score in the Study Eye   |        |        |        |
| Best corrected visual acuity (BCVA) at a starting test distance of 4 meters was measured using a set of three Precision Vision™ or Lighthouse distance acuity charts (modified ETDRS Charts 1, 2, and R). The BCVA letter score ranges from 0 to 100 (best score attainable), with a higher score indicating better visual acuity. |        |        |        |
| Units: ETDRS Letters   |        |        |        |
| arithmetic mean  | 58.7   | 58.9   |        |
| standard deviation   | ± 14.0 | ± 13.3 | -      |

## End points

### End points reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | Arm A: Faricimab   |
| Reporting group description:   |                    |
| Subjects randomized to Arm A received 6 mg of faricimab intravitreally (IVT) once every 4 weeks (Q4W) up to Week 12 (4 injections). At Week 20, protocol-defined assessment of disease activity required Arm A subjects with active disease to be treated with a once every 8 weeks (Q8W) dosing regimen of 6 mg of faricimab (i.e., at Weeks 20, 28, 36, 44, 52, and 60). A second assessment of disease activity at Week 24 required Arm A subjects with active disease (excluding those with active disease at Week 20) to be treated with a once every 12 weeks (Q12W) dosing regimen of 6 mg of faricimab IVT (i.e., at Weeks 24, 36, 48, and 60). Subjects who did not have active disease at Weeks 20 and 24 were treated with 6 mg of faricimab IVT once every 16 weeks (Q16W; i.e., at Weeks 28, 44, and 60). From Week 60 (when all of Arm A was scheduled to receive study drug) to Week 108, Arm A subjects were to be treated according to a personalized treatment interval (PTI) dosing regimen (Q8W, Q12W, or Q16W). |                    |
| Reporting group title  | Arm B: Aflibercept |
| Reporting group description:   |                    |
| Subjects randomized to the active comparator (Arm B) received a 2-mg dose of aflibercept that was administered intravitreally (IVT) Q8W, after 3 consecutive monthly doses during the 108-week treatment period. Subjects were to receive 15 IVT injections of aflibercept during the 108-week treatment period comprising three initiating injections (2 mg of aflibercept Q4W to Week 8), followed by 12 maintenance injections (2 mg of aflibercept Q8W at Weeks 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, and 104).  |                    |

### Primary: Change from Baseline in BCVA in the Study Eye Averaged Over Weeks 40, 44, and 48

|  |  |
|--|--|
| End point title  | Change from Baseline in BCVA in the Study Eye Averaged Over Weeks 40, 44, and 48 |
| End point description:   |  |
| Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. The Mixed Model of Repeated Measures (MMRM) analysis adjusted for treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), baseline BCVA ( $\geq 74$ , 73-55, and $\leq 54$ letters), baseline LLD ( $< 33$ and $\geq 33$ letters), and region (U.S. and Canada, Asia, and rest of the world). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. Invalid BCVA values were excluded from analysis. 95% CI is a rounding of 95.03% CI |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| From Baseline through Week 48  |  |

| End point values                          | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                        | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed               | 331                 | 327                   |  |  |
| Units: ETDRS Letters                      |                     |                       |  |  |
| arithmetic mean (confidence interval 95%) | 6.6 (5.3 to 7.8)    | 6.6 (5.3 to 7.8)      |  |  |



## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>   | Treatment Difference at Weeks 40-48   |
| Statistical analysis description:   |                                       |
| The null hypothesis, $H_0: \mu(\text{faricimab}) - \mu(\text{aflibercept}) \leq -4$ letters; the alternative hypothesis, $H_a: \mu(\text{faricimab}) - \mu(\text{aflibercept}) > -4$ letters. A sample size of approximately 320 participants in each arm provided greater than 90% power to show non-inferiority of faricimab to aflibercept in the change from baseline BCVA averaged over Weeks 40, 44, and 48 in the ITT population, using a non-inferiority margin of 4 letters at the one-sided 0.02485 significance level. |                                       |
| Comparison groups   | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis   | 658                                   |
| Analysis specification  | Pre-specified                         |
| Analysis type   | non-inferiority <sup>[1]</sup>        |
| Parameter estimate  | Adjusted mean difference              |
| Point estimate  | 0                                     |
| Confidence interval   |                                       |
| level   | 95 %                                  |
| sides   | 2-sided                               |
| lower limit   | -1.7                                  |
| upper limit   | 1.8                                   |
| Variability estimate  | Standard error of the mean            |
| Dispersion value  | 0.91                                  |

Notes:

[1] - If the lower bound of a two-sided 95.03% confidence interval (CI) for the difference in adjusted means of the two treatments (faricimab minus aflibercept) is greater than  $-4$  letters (the non-inferiority margin), then faricimab is considered non-inferior to aflibercept.

## Secondary: Change from Baseline in BCVA in the Study Eye Averaged Over Weeks 52, 56, and 60

|  |  |
|--|--|
| <b>End point title</b>   | Change from Baseline in BCVA in the Study Eye Averaged Over Weeks 52, 56, and 60 |
| End point description:   |  |
| Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. The Mixed Model of Repeated Measures (MMRM) analysis adjusted for treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), baseline BCVA ( $\geq 74$ , 73-55, and $\leq 54$ letters), baseline LLD ( $< 33$ and $\geq 33$ letters), and region (U.S. and Canada, Asia, and rest of the world). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. Invalid BCVA values were excluded from analysis. 95% CI is a rounding of 95.03% CI |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| From Baseline through Week 60  |  |

| End point values                          | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                        | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed               | 331                 | 327                   |  |  |
| Units: ETDRS Letters                      |                     |                       |  |  |
| arithmetic mean (confidence interval 95%) | 6.6 (5.3 to 7.9)    | 7.1 (5.8 to 8.4)      |  |  |

## Statistical analyses

| Statistical analysis title   | Treatment Difference at Weeks 52-60   |
|--|---------------------------------------|
| Statistical analysis description:  |                                       |
| The treatment difference in adjusted means of change from baseline BCVA is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. MMRM adjustments are listed in the outcome measure description. |                                       |
| Comparison groups  | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis  | 658                                   |
| Analysis specification   | Pre-specified                         |
| Analysis type  | other                                 |
| Parameter estimate   | Adjusted mean difference              |
| Point estimate   | -0.6                                  |
| Confidence interval  |                                       |
| level  | 95 %                                  |
| sides  | 2-sided                               |
| lower limit  | -2.4                                  |
| upper limit  | 1.3                                   |
| Variability estimate   | Standard error of the mean            |
| Dispersion value   | 0.93                                  |

## Secondary: Change from Baseline in BCVA in the Study Eye Over Time

| End point title  | Change from Baseline in BCVA in the Study Eye Over Time |
|--|---|
| End point description:   |   |
| Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. The Mixed Model of Repeated Measures (MMRM) analysis adjusted for treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), baseline BCVA ( $\geq 74$ , 73-55, and $\leq 54$ letters), baseline LLD ( $< 33$ and $\geq 33$ letters), and region (U.S. and Canada, Asia, and rest of the world). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. Invalid BCVA values were excluded from analysis. 95% CI is a rounding of 95.03% CI |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112   |   |

| End point values                          | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                        | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed               | 331                 | 327                   |  |  |
| Units: ETDRS Letters                      |                     |                       |  |  |
| arithmetic mean (confidence interval 95%) |                     |                       |  |  |
| Week 4                                    | 5.1 (4.2 to 5.9)    | 4.3 (3.5 to 5.2)      |  |  |
| Week 8                                    | 6.0 (5.1 to 6.9)    | 5.8 (4.9 to 6.8)      |  |  |
| Week 12                                   | 7.0 (6.1 to 8.0)    | 6.4 (5.4 to 7.4)      |  |  |
| Week 16                                   | 6.7 (5.6 to 7.7)    | 6.4 (5.4 to 7.4)      |  |  |
| Week 20                                   | 7.0 (5.9 to 8.1)    | 6.8 (5.7 to 7.9)      |  |  |
| Week 24                                   | 7.0 (5.8 to 8.1)    | 6.5 (5.4 to 7.6)      |  |  |
| Week 28                                   | 7.1 (5.9 to 8.2)    | 6.8 (5.6 to 7.9)      |  |  |
| Week 32                                   | 7.2 (6.0 to 8.3)    | 6.9 (5.7 to 8.0)      |  |  |
| Week 36                                   | 6.7 (5.5 to 7.9)    | 6.8 (5.6 to 8.0)      |  |  |
| Week 40                                   | 6.8 (5.5 to 8.1)    | 6.7 (5.4 to 8.0)      |  |  |
| Week 44                                   | 6.5 (5.3 to 7.8)    | 6.4 (5.2 to 7.7)      |  |  |
| Week 48                                   | 6.5 (5.1 to 7.8)    | 6.4 (5.0 to 7.7)      |  |  |
| Week 52                                   | 6.4 (5.1 to 7.7)    | 6.9 (5.5 to 8.3)      |  |  |
| Week 56                                   | 7.1 (5.7 to 8.4)    | 7.4 (6.0 to 8.7)      |  |  |
| Week 60                                   | 6.3 (4.9 to 7.7)    | 6.9 (5.5 to 8.3)      |  |  |
| Week 64                                   | 6.5 (5.1 to 8.0)    | 6.1 (4.7 to 7.6)      |  |  |
| Week 68                                   | 6.2 (4.8 to 7.6)    | 6.7 (5.3 to 8.1)      |  |  |
| Week 72                                   | 6.4 (4.9 to 7.8)    | 6.2 (4.8 to 7.7)      |  |  |
| Week 76                                   | 6.4 (4.9 to 7.9)    | 6.0 (4.6 to 7.5)      |  |  |
| Week 80                                   | 5.9 (4.4 to 7.4)    | 5.6 (4.1 to 7.2)      |  |  |
| Week 84                                   | 5.9 (4.3 to 7.5)    | 5.8 (4.2 to 7.3)      |  |  |
| Week 88                                   | 5.6 (4.1 to 7.1)    | 5.4 (3.9 to 7.0)      |  |  |
| Week 92                                   | 5.7 (4.2 to 7.2)    | 5.4 (3.9 to 7.0)      |  |  |
| Week 96                                   | 5.4 (3.9 to 7.0)    | 5.5 (3.9 to 7.0)      |  |  |
| Week 100                                  | 5.2 (3.6 to 6.8)    | 4.9 (3.3 to 6.5)      |  |  |
| Week 104                                  | 5.0 (3.4 to 6.6)    | 5.3 (3.7 to 6.9)      |  |  |
| Week 108                                  | 5.2 (3.5 to 6.8)    | 5.4 (3.7 to 7.0)      |  |  |
| Week 112                                  | 4.8 (3.2 to 6.5)    | 4.8 (3.1 to 6.5)      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Gaining Greater Than or Equal to ( $\geq$ )15, $\geq$ 10, $\geq$ 5, or $\geq$ 0 Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 40, 44, and 48

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Gaining Greater Than or Equal to ( $\geq$ )15, $\geq$ 10, $\geq$ 5, or $\geq$ 0 Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 40, 44, and 48 |
|-----------------|---|

### End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted percentage of

participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.03% CI.

|   |           |
|---|-----------|
| End point type                            | Secondary |
| End point timeframe:                      |           |
| Baseline, average of Weeks 40, 44, and 48 |           |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 302 <sup>[2]</sup>  | 291 <sup>[3]</sup>    |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Gaining $\geq 15$ Letters         | 20.2 (15.9 to 24.6) | 22.2 (17.7 to 26.8)   |  |  |
| Gaining $\geq 10$ Letters         | 39.2 (34.1 to 44.4) | 35.8 (30.6 to 40.9)   |  |  |
| Gaining $\geq 5$ Letters          | 60.5 (55.2 to 65.7) | 59.4 (53.9 to 64.9)   |  |  |
| Gaining $\geq 0$ Letters          | 82.2 (77.9 to 86.4) | 79.1 (74.5 to 83.6)   |  |  |

Notes:

[2] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

[3] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Gaining $\geq 15$ Letters at Weeks 40-48 |
| Statistical analysis description:  |  |
| The treatment difference in CMH weighted percentage of participants gaining $\geq 15$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |  |
| Comparison groups  | Arm A: Faricimab v Arm B: Aflibercept    |
| Number of subjects included in analysis  | 593                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | other                                    |
| Parameter estimate   | Difference in CMH Weighted Percentage    |
| Point estimate   | -2                                       |
| Confidence interval  |  |
| level  | 95 %                                     |
| sides  | 2-sided                                  |
| lower limit  | -8.3                                     |
| upper limit  | 4.3                                      |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Gaining $\geq 10$ Letters at Weeks 40-48 |
| Statistical analysis description:  |  |
| The treatment difference in CMH weighted percentage of participants gaining $\geq 10$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |  |
| Comparison groups  | Arm A: Faricimab v Arm B: Aflibercept    |

|   |                                       |
|---|---------------------------------------|
| Number of subjects included in analysis | 593                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Parameter estimate                      | Difference in CMH Weighted Percentage |
| Point estimate                          | 3.4                                   |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -3.9                                  |
| upper limit                             | 10.7                                  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Gaining $\geq 5$ Letters at Weeks 40-48 |
| Statistical analysis description:<br>The treatment difference in CMH weighted percentage of participants gaining $\geq 5$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |   |
| Comparison groups  | Arm A: Faricimab v Arm B: Aflibercept   |
| Number of subjects included in analysis  | 593                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | other                                   |
| Parameter estimate   | Difference in CMH Weighted Percentage   |
| Point estimate   | 1                                       |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -6.6                                    |
| upper limit  | 8.6                                     |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Gaining $\geq 0$ Letters at Weeks 40-48 |
| Statistical analysis description:<br>The treatment difference in CMH weighted percentage of participants gaining $\geq 0$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |   |
| Comparison groups  | Arm A: Faricimab v Arm B: Aflibercept   |
| Number of subjects included in analysis  | 593                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | other                                   |
| Parameter estimate   | Difference in CMH Weighted Percentage   |
| Point estimate   | 3.1                                     |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -3.1                                    |
| upper limit  | 9.3                                     |

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## Secondary: Percentage of Participants Gaining $\geq 15$ Letters from the Baseline BCVA

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## in the Study Eye Averaged Over Weeks 52, 56, and 60

|   |   |
|---|---|
| End point title   | Percentage of Participants Gaining $\geq 15$ Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 52, 56, and 60 |
| End point description:<br>BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$ letters, 73-55 letters, and $\leq 54$ letters), baseline LLD ( $\geq 33$ letters and $< 33$ letters), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.03% CI. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Baseline, average of Weeks 52, 56, and 60   |   |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 289 <sup>[4]</sup>  | 276 <sup>[5]</sup>    |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  | 22.6 (18.1 to 27.1) | 23.7 (19.1 to 28.4)   |  |  |

Notes:

[4] - Participants with at least one non-missing, valid assessment at Weeks 52, 56, or 60.

[5] - Participants with at least one non-missing, valid assessment at Weeks 52, 56, or 60.

## Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title  | Treatment Difference at Weeks 52-60   |
| Statistical analysis description:<br>The treatment difference in CMH weighted percentage of participants gaining $\geq 15$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |                                       |
| Comparison groups   | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis   | 565                                   |
| Analysis specification  | Pre-specified                         |
| Analysis type   | other                                 |
| Parameter estimate  | Difference in CMH Weighted Percentage |
| Point estimate  | -1.2                                  |
| Confidence interval   |                                       |
| level   | 95 %                                  |
| sides   | 2-sided                               |
| lower limit   | -7.7                                  |
| upper limit   | 5.3                                   |

## Secondary: Percentage of Participants Gaining $\geq 15$ Letters from the Baseline BCVA in the Study Eye Over Time

|   |  |
|---|--|
| End point title   | Percentage of Participants Gaining $\geq 15$ Letters from the Baseline BCVA in the Study Eye Over Time |
| End point description:  |  |
| <p>Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (<math>\geq 74</math> letters, 73-55 letters, and <math>\leq 54</math> letters), baseline LLD (<math>\geq 33</math> letters and <math>&lt; 33</math> letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.</p> |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112  |  |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[6]</sup>  | 327 <sup>[7]</sup>    |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 10.5 (7.2 to 13.7)  | 9.5 (6.4 to 12.6)     |  |  |
| Week 8 (n = 327, 322)             | 13.9 (10.3 to 17.5) | 13.5 (10.0 to 17.1)   |  |  |
| Week 12 (n = 326, 317)            | 17.7 (13.7 to 21.6) | 17.2 (13.3 to 21.1)   |  |  |
| Week 16 (n = 321, 315)            | 17.3 (13.3 to 21.3) | 17.7 (13.6 to 21.8)   |  |  |
| Week 20 (n = 320, 309)            | 20.2 (15.9 to 24.4) | 20.2 (15.9 to 24.4)   |  |  |
| Week 24 (n = 295, 288)            | 19.3 (14.9 to 23.6) | 18.9 (14.6 to 23.3)   |  |  |
| Week 28 (n = 292, 271)            | 23.7 (19.1 to 28.3) | 20.8 (16.1 to 25.4)   |  |  |
| Week 32 (n = 287, 288)            | 22.6 (18.0 to 27.2) | 19.5 (15.1 to 23.9)   |  |  |
| Week 36 (n = 293, 283)            | 22.2 (17.7 to 26.6) | 20.6 (16.1 to 25.0)   |  |  |
| Week 40 (n = 286, 288)            | 23.7 (19.0 to 28.3) | 25.4 (20.6 to 30.1)   |  |  |
| Week 44 (n = 285, 273)            | 21.5 (17.1 to 26.0) | 22.4 (17.7 to 27.1)   |  |  |
| Week 48 (n = 282, 277)            | 22.3 (17.7 to 26.9) | 23.1 (18.3 to 27.8)   |  |  |
| Week 52 (n = 283, 273)            | 22.7 (18.1 to 27.2) | 23.4 (18.7 to 28.1)   |  |  |
| Week 56 (n = 283, 273)            | 25.9 (21.1 to 30.7) | 27.0 (22.0 to 32.0)   |  |  |
| Week 60 (n = 278, 273)            | 22.6 (18.1 to 27.1) | 25.8 (20.9 to 30.7)   |  |  |
| Week 64 (n = 276, 266)            | 25.4 (20.6 to 30.2) | 21.2 (16.5 to 25.9)   |  |  |
| Week 68 (n = 276, 266)            | 24.5 (19.7 to 29.3) | 24.9 (20.0 to 29.8)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 72 (n = 276, 261)  | 22.6 (17.9 to 27.2) | 27.1 (22.0 to 32.1) |  |  |
| Week 76 (n = 268, 267)  | 22.1 (17.4 to 26.8) | 24.9 (20.1 to 29.8) |  |  |
| Week 80 (n = 275, 264)  | 22.9 (18.1 to 27.7) | 25.8 (20.8 to 30.7) |  |  |
| Week 84 (n = 279, 254)  | 23.7 (18.9 to 28.5) | 25.6 (20.6 to 30.6) |  |  |
| Week 88 (n = 276, 253)  | 24.1 (19.3 to 29.0) | 24.4 (19.5 to 29.3) |  |  |
| Week 92 (n = 273, 253)  | 22.5 (17.8 to 27.2) | 24.8 (19.9 to 29.8) |  |  |
| Week 96 (n = 266, 247)  | 25.7 (20.8 to 30.6) | 25.5 (20.5 to 30.6) |  |  |
| Week 100 (n = 272, 254) | 24.8 (19.9 to 29.8) | 23.1 (18.3 to 28.0) |  |  |
| Week 104 (n = 263, 249) | 22.5 (17.7 to 27.3) | 24.6 (19.6 to 29.5) |  |  |
| Week 108 (n = 267, 247) | 21.6 (16.8 to 26.3) | 22.3 (17.5 to 27.1) |  |  |
| Week 112 (n = 267, 254) | 25.2 (20.3 to 30.1) | 22.5 (17.8 to 27.1) |  |  |

Notes:

[6] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[7] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Gaining $\geq 10$ Letters from the Baseline BCVA in the Study Eye Over Time

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Gaining $\geq 10$ Letters from the Baseline BCVA in the Study Eye Over Time |
|-----------------|--|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112



| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[8]</sup>  | 327 <sup>[9]</sup>    |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 24.2 (19.8 to 28.7) | 22.1 (17.7 to 26.5)   |  |  |
| Week 8 (n = 327, 322)             | 32.4 (27.5 to 37.2) | 28.7 (24.1 to 33.4)   |  |  |
| Week 12 (n = 326, 317)            | 34.2 (29.3 to 39.1) | 34.6 (29.5 to 39.7)   |  |  |
| Week 16 (n = 321, 315)            | 35.3 (30.3 to 40.4) | 34.2 (29.2 to 39.3)   |  |  |
| Week 20 (n = 320, 309)            | 37.8 (32.7 to 42.9) | 34.3 (29.2 to 39.4)   |  |  |
| Week 24 (n = 295, 288)            | 39.2 (33.8 to 44.5) | 35.2 (29.9 to 40.5)   |  |  |
| Week 28 (n = 292, 271)            | 40.5 (35.1 to 45.8) | 36.0 (30.5 to 41.4)   |  |  |
| Week 32 (n = 287, 288)            | 40.5 (35.1 to 46.0) | 35.0 (29.7 to 40.3)   |  |  |
| Week 36 (n = 293, 283)            | 38.9 (33.6 to 44.2) | 38.9 (33.5 to 44.3)   |  |  |
| Week 40 (n = 286, 288)            | 40.9 (35.5 to 46.3) | 39.3 (34.0 to 44.7)   |  |  |
| Week 44 (n = 285, 273)            | 42.3 (36.8 to 47.8) | 39.5 (34.1 to 45.0)   |  |  |
| Week 48 (n = 282, 277)            | 41.0 (35.5 to 46.5) | 38.6 (33.2 to 43.9)   |  |  |
| Week 52 (n = 283, 273)            | 44.2 (38.8 to 49.7) | 42.1 (36.6 to 47.6)   |  |  |
| Week 56 (n = 283, 273)            | 44.2 (38.8 to 49.7) | 43.6 (38.1 to 49.2)   |  |  |
| Week 60 (n = 278, 273)            | 43.1 (37.6 to 48.6) | 42.4 (36.8 to 47.9)   |  |  |
| Week 64 (n = 276, 266)            | 44.0 (38.5 to 49.5) | 41.1 (35.4 to 46.8)   |  |  |
| Week 68 (n = 276, 266)            | 40.1 (34.7 to 45.5) | 40.7 (35.3 to 46.2)   |  |  |
| Week 72 (n = 276, 261)            | 42.0 (36.5 to 47.4) | 38.9 (33.4 to 44.3)   |  |  |
| Week 76 (n = 268, 267)            | 42.2 (36.7 to 47.8) | 40.7 (35.1 to 46.2)   |  |  |
| Week 80 (n = 275, 264)            | 44.2 (38.6 to 49.9) | 41.9 (36.2 to 47.6)   |  |  |
| Week 84 (n = 279, 254)            | 42.7 (37.2 to 48.3) | 41.4 (35.6 to 47.2)   |  |  |
| Week 88 (n = 276, 253)            | 40.3 (34.8 to 45.9) | 39.4 (33.7 to 45.1)   |  |  |
| Week 92 (n = 273, 253)            | 42.1 (36.5 to 47.8) | 41.0 (35.3 to 46.7)   |  |  |
| Week 96 (n = 266, 247)            | 41.1 (35.5 to 46.7) | 39.1 (33.3 to 45.0)   |  |  |
| Week 100 (n = 272, 254)           | 40.2 (34.6 to 45.7) | 34.6 (29.0 to 40.1)   |  |  |
| Week 104 (n = 263, 249)           | 44.0 (38.3 to 49.7) | 36.2 (30.5 to 41.9)   |  |  |
| Week 108 (n = 267, 247)           | 41.7 (36.0 to 47.4) | 38.0 (32.2 to 43.8)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 112 (n = 267, 254) | 41.3 (35.7 to 47.0) | 35.0 (29.6 to 40.5) |  |  |
|-------------------------|---------------------|---------------------|--|--|

Notes:

[8] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[9] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Gaining ≥5 Letters from the Baseline BCVA in the Study Eye Over Time

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Gaining ≥5 Letters from the Baseline BCVA in the Study Eye Over Time |
|-----------------|---|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥74 letters, 73-55 letters, and ≤54 letters), baseline LLD (≥33 letters and <33 letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[10]</sup> | 327 <sup>[11]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 47.8 (42.6 to 53.0) | 47.5 (42.2 to 52.8)   |  |  |
| Week 8 (n = 327, 322)             | 56.8 (51.6 to 62.0) | 54.6 (49.3 to 59.8)   |  |  |
| Week 12 (n = 326, 317)            | 63.9 (58.9 to 68.9) | 57.6 (52.3 to 62.9)   |  |  |
| Week 16 (n = 321, 315)            | 61.7 (56.5 to 66.8) | 59.6 (54.3 to 64.9)   |  |  |
| Week 20 (n = 320, 309)            | 64.1 (59.0 to 69.2) | 60.9 (55.6 to 66.3)   |  |  |
| Week 24 (n = 295, 288)            | 62.2 (56.8 to 67.6) | 60.2 (54.7 to 65.7)   |  |  |
| Week 28 (n = 292, 271)            | 63.6 (58.2 to 68.9) | 60.5 (54.8 to 66.2)   |  |  |
| Week 32 (n = 287, 288)            | 63.3 (58.0 to 68.7) | 60.1 (54.6 to 65.6)   |  |  |
| Week 36 (n = 293, 283)            | 61.4 (56.0 to 66.9) | 60.4 (54.9 to 65.9)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 40 (n = 286, 288)  | 63.5 (58.1 to 68.9) | 60.9 (55.5 to 66.4) |  |  |
| Week 44 (n = 285, 273)  | 60.1 (54.6 to 65.6) | 62.3 (56.7 to 67.8) |  |  |
| Week 48 (n = 282, 277)  | 60.0 (54.5 to 65.6) | 63.5 (57.9 to 69.1) |  |  |
| Week 52 (n = 283, 273)  | 63.5 (58.1 to 69.0) | 67.2 (61.7 to 72.6) |  |  |
| Week 56 (n = 283, 273)  | 64.1 (58.7 to 69.5) | 66.5 (61.0 to 72.0) |  |  |
| Week 60 (n = 278, 273)  | 61.6 (56.1 to 67.2) | 65.5 (59.9 to 71.0) |  |  |
| Week 64 (n = 276, 266)  | 65.2 (59.8 to 70.6) | 63.1 (57.5 to 68.8) |  |  |
| Week 68 (n = 276, 266)  | 63.0 (57.4 to 68.5) | 64.0 (58.5 to 69.6) |  |  |
| Week 72 (n = 276, 261)  | 64.1 (58.6 to 69.6) | 66.6 (60.9 to 72.2) |  |  |
| Week 76 (n = 268, 267)  | 63.9 (58.2 to 69.6) | 58.7 (53.0 to 64.4) |  |  |
| Week 80 (n = 275, 264)  | 63.3 (57.7 to 68.9) | 62.3 (56.6 to 67.9) |  |  |
| Week 84 (n = 279, 254)  | 61.6 (56.1 to 67.2) | 64.3 (58.6 to 70.1) |  |  |
| Week 88 (n = 276, 253)  | 62.6 (57.1 to 68.1) | 60.7 (54.9 to 66.5) |  |  |
| Week 92 (n = 273, 253)  | 62.7 (57.1 to 68.3) | 58.3 (52.6 to 64.0) |  |  |
| Week 96 (n = 266, 247)  | 61.3 (55.6 to 67.0) | 61.0 (55.1 to 67.0) |  |  |
| Week 100 (n = 272, 254) | 61.7 (56.1 to 67.3) | 56.9 (50.9 to 62.9) |  |  |
| Week 104 (n = 263, 249) | 60.3 (54.6 to 66.0) | 59.3 (53.3 to 65.3) |  |  |
| Week 108 (n = 267, 247) | 62.4 (56.8 to 68.0) | 58.0 (51.8 to 64.1) |  |  |
| Week 112 (n = 267, 254) | 59.9 (54.2 to 65.6) | 59.4 (53.4 to 65.3) |  |  |

Notes:

[10] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[11] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Gaining $\geq 0$ Letters from the Baseline BCVA in the Study Eye Over Time

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Gaining $\geq 0$ Letters from the Baseline BCVA in the Study Eye Over Time |
|-----------------|---|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112 |           |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[12]</sup> | 327 <sup>[13]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 80.5 (76.3 to 84.7) | 74.2 (69.5 to 78.9)   |  |  |
| Week 8 (n = 327, 322)             | 82.3 (78.3 to 86.3) | 80.3 (76.0 to 84.5)   |  |  |
| Week 12 (n = 326, 317)            | 84.1 (80.3 to 88.0) | 81.0 (76.8 to 85.1)   |  |  |
| Week 16 (n = 321, 315)            | 82.6 (78.5 to 86.6) | 83.0 (78.9 to 87.0)   |  |  |
| Week 20 (n = 320, 309)            | 84.8 (80.9 to 88.6) | 83.1 (79.1 to 87.2)   |  |  |
| Week 24 (n = 295, 288)            | 82.8 (78.6 to 86.9) | 82.0 (77.6 to 86.4)   |  |  |
| Week 28 (n = 292, 271)            | 82.7 (78.5 to 86.8) | 83.0 (78.7 to 87.4)   |  |  |
| Week 32 (n = 287, 288)            | 80.3 (75.9 to 84.7) | 82.2 (77.8 to 86.5)   |  |  |
| Week 36 (n = 293, 283)            | 81.2 (76.8 to 85.6) | 76.5 (71.7 to 81.3)   |  |  |
| Week 40 (n = 286, 288)            | 82.0 (77.6 to 86.3) | 77.6 (72.9 to 82.3)   |  |  |
| Week 44 (n = 285, 273)            | 84.0 (79.8 to 88.2) | 78.6 (73.9 to 83.2)   |  |  |
| Week 48 (n = 282, 277)            | 82.7 (78.3 to 87.1) | 78.9 (74.1 to 83.6)   |  |  |
| Week 52 (n = 283, 273)            | 79.4 (74.8 to 84.0) | 84.7 (80.5 to 88.9)   |  |  |
| Week 56 (n = 283, 273)            | 80.7 (76.1 to 85.2) | 82.6 (78.2 to 87.0)   |  |  |
| Week 60 (n = 278, 273)            | 78.9 (74.2 to 83.6) | 81.5 (77.0 to 86.0)   |  |  |
| Week 64 (n = 276, 266)            | 81.3 (76.8 to 85.8) | 81.1 (76.5 to 85.7)   |  |  |
| Week 68 (n = 276, 266)            | 80.5 (76.0 to 85.1) | 80.4 (75.8 to 85.0)   |  |  |
| Week 72 (n = 276, 261)            | 79.5 (74.8 to 84.1) | 78.8 (74.0 to 83.6)   |  |  |
| Week 76 (n = 268, 267)            | 81.0 (76.4 to 85.6) | 79.8 (75.2 to 84.5)   |  |  |
| Week 80 (n = 275, 264)            | 80.0 (75.3 to 84.7) | 76.0 (71.0 to 81.1)   |  |  |
| Week 84 (n = 279, 254)            | 78.7 (73.9 to 83.5) | 81.0 (76.3 to 85.7)   |  |  |
| Week 88 (n = 276, 253)            | 78.7 (73.9 to 83.5) | 80.6 (75.9 to 85.4)   |  |  |
| Week 92 (n = 273, 253)            | 81.3 (76.7 to 85.8) | 76.3 (71.2 to 81.4)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 96 (n = 266, 247)  | 76.3 (71.3 to 81.3) | 77.5 (72.5 to 82.6) |  |  |
| Week 100 (n = 272, 254) | 75.7 (70.8 to 80.7) | 74.8 (69.6 to 80.0) |  |  |
| Week 104 (n = 263, 249) | 76.6 (71.6 to 81.6) | 79.0 (74.0 to 84.0) |  |  |
| Week 108 (n = 267, 247) | 78.8 (74.0 to 83.6) | 76.9 (71.7 to 82.1) |  |  |
| Week 112 (n = 267, 254) | 74.6 (69.5 to 79.8) | 77.4 (72.3 to 82.5) |  |  |

Notes:

[12] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[13] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Avoiding a Loss of $\geq 15$ , $\geq 10$ , or $\geq 5$ Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 40, 44, and 48

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Avoiding a Loss of $\geq 15$ , $\geq 10$ , or $\geq 5$ Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 40, 44, and 48 |
|-----------------|--|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, average of Weeks 40, 44, and 48

| End point values                     | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|--------------------------------------|---------------------|-----------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed          | 302 <sup>[14]</sup> | 291 <sup>[15]</sup>   |  |  |
| Units: Percentage of participants    |                     |                       |  |  |
| number (confidence interval 95%)     |                     |                       |  |  |
| Avoiding a Loss of $\geq 15$ Letters | 95.8 (93.6 to 98.0) | 97.3 (95.5 to 99.1)   |  |  |
| Avoiding a Loss of $\geq 10$ Letters | 93.8 (91.1 to 96.4) | 94.6 (92.2 to 97.1)   |  |  |
| Avoiding a Loss of $\geq 5$ Letters  | 91.2 (88.0 to 94.3) | 88.5 (85.0 to 92.0)   |  |  |

Notes:

[14] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

[15] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Avoiding a Loss of $\geq 15$ Letters at Weeks 40-48 |
| Statistical analysis description:   |   |
| The treatment difference in CMH weighted percentage of participants avoiding a loss of $\geq 15$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |   |
| Comparison groups   | Arm A: Faricimab v Arm B: Aflibercept               |
| Number of subjects included in analysis   | 593   |
| Analysis specification  | Pre-specified                                       |
| Analysis type   | other   |
| Parameter estimate  | Difference in CMH Weighted Percentage               |
| Point estimate  | -1.5  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | -4.4  |
| upper limit   | 1.3   |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Avoiding a Loss of $\geq 5$ Letters at Weeks 40-48 |
| Statistical analysis description:  |  |
| The treatment difference in CMH weighted percentage of participants avoiding a loss of $\geq 5$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |  |
| Comparison groups  | Arm A: Faricimab v Arm B: Aflibercept              |
| Number of subjects included in analysis  | 593  |
| Analysis specification   | Pre-specified                                      |
| Analysis type  | other  |
| Parameter estimate   | Difference in CMH Weighted Percentage              |
| Point estimate   | 2.6  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | -2.1   |
| upper limit  | 7.3  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Avoiding a Loss of $\geq 10$ Letters at Weeks 40-48 |
| Statistical analysis description:   |   |
| The treatment difference in CMH weighted percentage of participants avoiding a loss of $\geq 10$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |   |
| Comparison groups   | Arm A: Faricimab v Arm B: Aflibercept               |
| Number of subjects included in analysis   | 593   |
| Analysis specification  | Pre-specified                                       |
| Analysis type   | other   |
| Parameter estimate  | Difference in CMH Weighted Percentage               |
| Point estimate  | -0.9  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | -4.5  |
| upper limit   | 2.8   |

## Secondary: Percentage of Participants Avoiding a Loss of $\geq 15$ Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 52, 56, and 60

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Avoiding a Loss of $\geq 15$ Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 52, 56, and 60 |
|-----------------|--|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, average of Weeks 52, 56, and 60

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 289 <sup>[16]</sup> | 276 <sup>[17]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  | 96.5 (94.4 to 98.6) | 96.1 (94.0 to 98.3)   |  |  |

Notes:

[16] - Participants with at least one non-missing, valid assessment at Weeks 52, 56, or 60.

[17] - Participants with at least one non-missing, valid assessment at Weeks 52, 56, or 60.

## Statistical analyses

|                            |                                     |
|----------------------------|-------------------------------------|
| Statistical analysis title | Treatment Difference at Weeks 52-60 |
|----------------------------|-------------------------------------|

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants avoiding a loss of  $\geq 15$  letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept.

|   |                                       |
|---|---------------------------------------|
| Comparison groups                       | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis | 565                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Parameter estimate                      | Difference in CMH Weighted Percentage |
| Point estimate                          | 0.4                                   |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -2.6                                  |
| upper limit                             | 3.3                                   |

## Secondary: Percentage of Participants Avoiding a Loss of $\geq 15$ Letters from the Baseline BCVA in the Study Eye Over Time

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Avoiding a Loss of $\geq 15$ Letters from the Baseline BCVA in the Study Eye Over Time |
|-----------------|---|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted percentage of participants avoiding a loss of letters in BCVA from baseline was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab  | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|----------------------|-----------------------|--|--|
| Subject group type                | Reporting group      | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[18]</sup>  | 327 <sup>[19]</sup>   |  |  |
| Units: Percentage of participants |                      |                       |  |  |
| number (confidence interval 95%)  |                      |                       |  |  |
| Week 4 (n = 328, 323)             | 99.4 (98.6 to 100.0) | 98.1 (96.7 to 99.6)   |  |  |
| Week 8 (n = 327, 322)             | 98.5 (97.3 to 99.8)  | 97.8 (96.3 to 99.4)   |  |  |
| Week 12 (n = 326, 317)            | 98.5 (97.3 to 99.8)  | 98.1 (96.7 to 99.6)   |  |  |
| Week 16 (n = 321, 315)            | 97.6 (96.0 to 99.2)  | 98.4 (97.0 to 99.8)   |  |  |
| Week 20 (n = 320, 309)            | 97.3 (95.5 to 99.0)  | 98.4 (97.0 to 99.7)   |  |  |
| Week 24 (n = 295, 288)            | 96.6 (94.6 to 98.6)  | 97.2 (95.4 to 99.1)   |  |  |
| Week 28 (n = 292, 271)            | 97.0 (95.1 to 98.9)  | 97.8 (96.2 to 99.5)   |  |  |
| Week 32 (n = 287, 288)            | 97.0 (95.1 to 98.9)  | 96.9 (95.0 to 98.9)   |  |  |
| Week 36 (n = 293, 283)            | 97.0 (95.2 to 98.9)  | 96.5 (94.5 to 98.6)   |  |  |
| Week 40 (n = 286, 288)            | 96.2 (94.1 to 98.4)  | 97.6 (95.9 to 99.3)   |  |  |
| Week 44 (n = 285, 273)            | 95.9 (93.6 to 98.1)  | 96.4 (94.3 to 98.5)   |  |  |
| Week 48 (n = 282, 277)            | 95.8 (93.5 to 98.0)  | 96.9 (95.0 to 98.8)   |  |  |
| Week 52 (n = 283, 273)            | 94.9 (92.5 to 97.4)  | 96.8 (94.8 to 98.8)   |  |  |
| Week 56 (n = 283, 273)            | 96.1 (93.9 to 98.3)  | 96.8 (94.8 to 98.8)   |  |  |



|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 60 (n = 278, 273)  | 95.0 (92.5 to 97.5) | 96.1 (94.0 to 98.3) |  |  |
| Week 64 (n = 276, 266)  | 96.4 (94.3 to 98.5) | 94.9 (92.3 to 97.4) |  |  |
| Week 68 (n = 276, 266)  | 94.7 (92.1 to 97.2) | 96.0 (93.7 to 98.3) |  |  |
| Week 72 (n = 276, 261)  | 94.5 (91.9 to 97.2) | 95.4 (92.9 to 97.9) |  |  |
| Week 76 (n = 268, 267)  | 94.9 (92.3 to 97.4) | 93.7 (90.9 to 96.6) |  |  |
| Week 80 (n = 275, 264)  | 93.9 (91.1 to 96.6) | 93.3 (90.4 to 96.3) |  |  |
| Week 84 (n = 279, 254)  | 92.5 (89.5 to 95.5) | 93.8 (90.9 to 96.7) |  |  |
| Week 88 (n = 276, 253)  | 94.1 (91.4 to 96.7) | 94.3 (91.5 to 97.0) |  |  |
| Week 92 (n = 273, 253)  | 93.0 (90.2 to 95.9) | 94.6 (92.0 to 97.2) |  |  |
| Week 96 (n = 266, 247)  | 92.6 (89.6 to 95.6) | 95.0 (92.5 to 97.6) |  |  |
| Week 100 (n = 272, 254) | 92.5 (89.5 to 95.5) | 93.9 (91.1 to 96.7) |  |  |
| Week 104 (n = 263, 249) | 92.9 (90.0 to 95.9) | 94.0 (91.0 to 96.9) |  |  |
| Week 108 (n = 267, 247) | 92.3 (89.2 to 95.3) | 93.3 (90.3 to 96.3) |  |  |
| Week 112 (n = 267, 254) | 91.8 (88.7 to 95.0) | 93.0 (89.9 to 96.1) |  |  |

Notes:

[18] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[19] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Avoiding a Loss of $\geq 10$ Letters from the Baseline BCVA in the Study Eye Over Time

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Avoiding a Loss of $\geq 10$ Letters from the Baseline BCVA in the Study Eye Over Time |
|-----------------|---|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted percentage of participants avoiding a loss of letters in BCVA from baseline was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[20]</sup> | 327 <sup>[21]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 98.5 (97.2 to 99.8) | 96.2 (94.1 to 98.3)   |  |  |
| Week 8 (n = 327, 322)             | 97.0 (95.3 to 98.7) | 96.9 (95.0 to 98.7)   |  |  |
| Week 12 (n = 326, 317)            | 97.0 (95.2 to 98.8) | 96.8 (94.9 to 98.7)   |  |  |
| Week 16 (n = 321, 315)            | 96.6 (94.7 to 98.5) | 96.8 (94.9 to 98.7)   |  |  |
| Week 20 (n = 320, 309)            | 95.2 (92.9 to 97.4) | 96.1 (94.0 to 98.2)   |  |  |
| Week 24 (n = 295, 288)            | 95.2 (92.9 to 97.6) | 95.5 (93.2 to 97.8)   |  |  |
| Week 28 (n = 292, 271)            | 95.0 (92.6 to 97.4) | 95.2 (92.7 to 97.7)   |  |  |
| Week 32 (n = 287, 288)            | 94.6 (92.1 to 97.1) | 95.9 (93.7 to 98.1)   |  |  |
| Week 36 (n = 293, 283)            | 95.3 (93.0 to 97.7) | 94.4 (91.8 to 97.0)   |  |  |
| Week 40 (n = 286, 288)            | 93.8 (91.1 to 96.5) | 94.6 (92.2 to 97.1)   |  |  |
| Week 44 (n = 285, 273)            | 94.1 (91.4 to 96.8) | 92.1 (89.1 to 95.1)   |  |  |
| Week 48 (n = 282, 277)            | 92.2 (89.2 to 95.3) | 94.8 (92.3 to 97.3)   |  |  |
| Week 52 (n = 283, 273)            | 91.4 (88.2 to 94.6) | 93.8 (91.1 to 96.6)   |  |  |
| Week 56 (n = 283, 273)            | 93.3 (90.5 to 96.2) | 95.0 (92.5 to 97.5)   |  |  |
| Week 60 (n = 278, 273)            | 91.4 (88.2 to 94.6) | 93.2 (90.4 to 96.1)   |  |  |
| Week 64 (n = 276, 266)            | 93.5 (90.7 to 96.4) | 92.3 (89.3 to 95.4)   |  |  |
| Week 68 (n = 276, 266)            | 91.9 (88.8 to 95.0) | 92.9 (89.9 to 96.0)   |  |  |
| Week 72 (n = 276, 261)            | 92.4 (89.3 to 95.5) | 91.6 (88.3 to 94.9)   |  |  |
| Week 76 (n = 268, 267)            | 93.1 (90.2 to 96.0) | 90.1 (86.5 to 93.6)   |  |  |
| Week 80 (n = 275, 264)            | 92.1 (89.0 to 95.2) | 89.9 (86.3 to 93.5)   |  |  |
| Week 84 (n = 279, 254)            | 90.3 (86.9 to 93.7) | 91.8 (88.4 to 95.1)   |  |  |
| Week 88 (n = 276, 253)            | 90.8 (87.5 to 94.1) | 92.3 (89.1 to 95.4)   |  |  |
| Week 92 (n = 273, 253)            | 90.7 (87.4 to 94.1) | 91.0 (87.6 to 94.5)   |  |  |
| Week 96 (n = 266, 247)            | 90.4 (87.0 to 93.8) | 92.6 (89.4 to 95.8)   |  |  |
| Week 100 (n = 272, 254)           | 90.7 (87.4 to 94.0) | 91.6 (88.3 to 94.9)   |  |  |
| Week 104 (n = 263, 249)           | 89.0 (85.4 to 92.7) | 92.2 (88.9 to 95.4)   |  |  |
| Week 108 (n = 267, 247)           | 88.5 (84.8 to 92.3) | 91.2 (87.7 to 94.7)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 112 (n = 267, 254) | 88.5 (84.7 to 92.2) | 89.5 (85.8 to 93.2) |  |  |
|-------------------------|---------------------|---------------------|--|--|

Notes:

[20] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[21] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Avoiding a Loss of $\geq 5$ Letters from the Baseline BCVA in the Study Eye Over Time

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Avoiding a Loss of $\geq 5$ Letters from the Baseline BCVA in the Study Eye Over Time |
|-----------------|--|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted percentage of participants avoiding a loss of letters in BCVA from baseline was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[22]</sup> | 327 <sup>[23]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 93.0 (90.4 to 95.6) | 91.8 (88.9 to 94.7)   |  |  |
| Week 8 (n = 327, 322)             | 93.1 (90.4 to 95.7) | 94.1 (91.5 to 96.6)   |  |  |
| Week 12 (n = 326, 317)            | 93.3 (90.7 to 95.9) | 91.8 (88.8 to 94.7)   |  |  |
| Week 16 (n = 321, 315)            | 91.7 (88.7 to 94.6) | 90.8 (87.7 to 94.0)   |  |  |
| Week 20 (n = 320, 309)            | 92.0 (89.1 to 94.9) | 92.9 (90.0 to 95.7)   |  |  |
| Week 24 (n = 295, 288)            | 90.6 (87.4 to 93.9) | 91.7 (88.6 to 94.8)   |  |  |
| Week 28 (n = 292, 271)            | 91.0 (87.9 to 94.1) | 90.2 (86.7 to 93.7)   |  |  |
| Week 32 (n = 287, 288)            | 89.9 (86.5 to 93.2) | 91.0 (87.7 to 94.3)   |  |  |
| Week 36 (n = 293, 283)            | 90.7 (87.5 to 94.0) | 87.4 (83.6 to 91.2)   |  |  |
| Week 40 (n = 286, 288)            | 91.7 (88.6 to 94.9) | 88.1 (84.5 to 91.7)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 44 (n = 285, 273)  | 90.9 (87.7 to 94.2) | 88.8 (85.3 to 92.3) |  |  |
| Week 48 (n = 282, 277)  | 89.4 (85.9 to 93.0) | 88.6 (85.0 to 92.2) |  |  |
| Week 52 (n = 283, 273)  | 88.9 (85.3 to 92.5) | 91.7 (88.6 to 94.8) |  |  |
| Week 56 (n = 283, 273)  | 89.5 (86.0 to 93.0) | 88.8 (85.2 to 92.5) |  |  |
| Week 60 (n = 278, 273)  | 86.7 (82.9 to 90.6) | 88.8 (85.2 to 92.4) |  |  |
| Week 64 (n = 276, 266)  | 87.8 (84.1 to 91.6) | 86.0 (82.0 to 90.1) |  |  |
| Week 68 (n = 276, 266)  | 88.2 (84.5 to 91.9) | 87.1 (83.2 to 91.0) |  |  |
| Week 72 (n = 276, 261)  | 87.0 (83.1 to 90.9) | 87.3 (83.4 to 91.2) |  |  |
| Week 76 (n = 268, 267)  | 87.1 (83.2 to 91.1) | 85.4 (81.2 to 89.5) |  |  |
| Week 80 (n = 275, 264)  | 87.3 (83.5 to 91.2) | 82.8 (78.3 to 87.3) |  |  |
| Week 84 (n = 279, 254)  | 84.1 (79.9 to 88.4) | 87.1 (83.1 to 91.2) |  |  |
| Week 88 (n = 276, 253)  | 87.5 (83.7 to 91.3) | 86.6 (82.5 to 90.6) |  |  |
| Week 92 (n = 273, 253)  | 87.0 (83.1 to 90.9) | 87.2 (83.2 to 91.2) |  |  |
| Week 96 (n = 266, 247)  | 82.7 (78.4 to 87.1) | 86.2 (82.1 to 90.4) |  |  |
| Week 100 (n = 272, 254) | 85.9 (81.9 to 89.8) | 84.2 (79.9 to 88.5) |  |  |
| Week 104 (n = 263, 249) | 83.5 (79.1 to 87.8) | 85.4 (81.1 to 89.7) |  |  |
| Week 108 (n = 267, 247) | 84.1 (79.9 to 88.4) | 83.9 (79.4 to 88.5) |  |  |
| Week 112 (n = 267, 254) | 82.2 (77.7 to 86.7) | 84.4 (80.0 to 88.8) |  |  |

Notes:

[22] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[23] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Gaining ≥15 Letters from the Baseline BCVA or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Averaged Over Weeks 40, 44, and 48

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Gaining ≥15 Letters from the Baseline BCVA or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Averaged Over Weeks 40, 44, and 48 |
|-----------------|--|

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥74 letters, 73-55 letters, and ≤54 letters), baseline LLD (≥33 letters and <33 letters), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.03% CI.

|   |           |
|---|-----------|
| End point type                            | Secondary |
| End point timeframe:                      |           |
| Baseline, average of Weeks 40, 44, and 48 |           |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 302 <sup>[24]</sup> | 291 <sup>[25]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  | 24.5 (19.8 to 29.2) | 26.2 (21.2 to 31.1)   |  |  |

Notes:

[24] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

[25] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

## Statistical analyses

| Statistical analysis title   | Treatment Difference at Weeks 40-48   |
|--|---------------------------------------|
| Statistical analysis description:  |                                       |
| The treatment difference in CMH weighted percentage of participants gaining $\geq 15$ letters or achieving BCVA $\geq 84$ letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. |                                       |
| Comparison groups  | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis  | 593                                   |
| Analysis specification   | Pre-specified                         |
| Analysis type  | other                                 |
| Parameter estimate   | Difference in CMH Weighted Percentage |
| Point estimate   | -1.7                                  |
| Confidence interval  |                                       |
| level  | 95 %                                  |
| sides  | 2-sided                               |
| lower limit  | -8.5                                  |
| upper limit  | 5.1                                   |

## Secondary: Percentage of Participants Gaining $\geq 15$ Letters from the Baseline BCVA or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA $\geq 84$ Letters) in the Study Eye Over Time

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Gaining $\geq 15$ Letters from the Baseline BCVA or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA $\geq 84$ Letters) in the Study Eye Over Time |
|-----------------|---|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[26]</sup> | 327 <sup>[27]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 11.3 (7.9 to 14.6)  | 12.4 (8.9 to 15.9)    |  |  |
| Week 8 (n = 327, 322)             | 16.5 (12.5 to 20.4) | 16.1 (12.2 to 20.0)   |  |  |
| Week 12 (n = 326, 317)            | 22.0 (17.7 to 26.4) | 21.1 (16.7 to 25.4)   |  |  |
| Week 16 (n = 321, 315)            | 21.7 (17.4 to 26.1) | 20.7 (16.2 to 25.1)   |  |  |
| Week 20 (n = 320, 309)            | 24.9 (20.2 to 29.5) | 24.9 (20.2 to 29.6)   |  |  |
| Week 24 (n = 295, 288)            | 23.6 (18.9 to 28.3) | 23.7 (18.9 to 28.6)   |  |  |
| Week 28 (n = 292, 271)            | 27.7 (22.7 to 32.7) | 26.9 (21.8 to 32.1)   |  |  |
| Week 32 (n = 287, 288)            | 28.7 (23.6 to 33.8) | 23.2 (18.4 to 27.9)   |  |  |
| Week 36 (n = 293, 283)            | 25.9 (21.1 to 30.7) | 24.6 (19.7 to 29.5)   |  |  |
| Week 40 (n = 286, 288)            | 27.9 (22.9 to 32.9) | 31.1 (25.9 to 36.4)   |  |  |
| Week 44 (n = 285, 273)            | 27.2 (22.2 to 32.1) | 28.1 (22.8 to 33.3)   |  |  |
| Week 48 (n = 282, 277)            | 27.3 (22.3 to 32.4) | 28.3 (23.1 to 33.6)   |  |  |
| Week 52 (n = 283, 273)            | 29.2 (24.1 to 34.3) | 28.3 (23.1 to 33.5)   |  |  |
| Week 56 (n = 283, 273)            | 32.0 (26.7 to 37.2) | 31.5 (26.1 to 36.9)   |  |  |
| Week 60 (n = 278, 273)            | 27.5 (22.5 to 32.5) | 31.4 (26.0 to 36.8)   |  |  |
| Week 64 (n = 276, 266)            | 30.1 (25.0 to 35.3) | 27.1 (21.9 to 32.3)   |  |  |
| Week 68 (n = 276, 266)            | 28.3 (23.1 to 33.4) | 30.0 (24.6 to 35.3)   |  |  |
| Week 72 (n = 276, 261)            | 26.4 (21.4 to 31.4) | 31.5 (26.0 to 36.9)   |  |  |
| Week 76 (n = 268, 267)            | 27.4 (22.2 to 32.5) | 29.2 (23.9 to 34.4)   |  |  |
| Week 80 (n = 275, 264)            | 28.7 (23.4 to 34.0) | 31.2 (25.7 to 36.6)   |  |  |
| Week 84 (n = 279, 254)            | 28.0 (22.8 to 33.1) | 30.1 (24.6 to 35.5)   |  |  |
| Week 88 (n = 276, 253)            | 29.1 (23.8 to 34.4) | 28.4 (23.2 to 33.6)   |  |  |
| Week 92 (n = 273, 253)            | 27.0 (21.8 to 32.1) | 29.0 (23.6 to 34.3)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 96 (n = 266, 247)  | 30.7 (25.3 to 36.0) | 31.1 (25.5 to 36.6) |  |  |
| Week 100 (n = 272, 254) | 28.6 (23.3 to 33.9) | 27.2 (22.0 to 32.5) |  |  |
| Week 104 (n = 263, 249) | 27.2 (22.0 to 32.4) | 30.2 (24.8 to 35.6) |  |  |
| Week 108 (n = 267, 247) | 26.3 (21.1 to 31.4) | 27.0 (21.7 to 32.4) |  |  |
| Week 112 (n = 267, 254) | 29.4 (24.1 to 34.7) | 26.5 (21.4 to 31.6) |  |  |

Notes:

[26] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[27] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA $\geq$ 69 Letters) in the Study Eye Averaged Over Weeks 40, 44, and 48

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA $\geq$ 69 Letters) in the Study Eye Averaged Over Weeks 40, 44, and 48 |
|-----------------|---|

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (<69 letters vs.  $\geq$ 69 letters), baseline LLD ( $\geq$ 33 letters and <33 letters), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, average of Weeks 40, 44, and 48

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 302 <sup>[28]</sup> | 291 <sup>[29]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  | 55.2 (50.1 to 60.2) | 49.4 (44.4 to 54.4)   |  |  |

Notes:

[28] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

[29] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

## Statistical analyses

|                            |                                     |
|----------------------------|-------------------------------------|
| Statistical analysis title | Treatment Difference at Weeks 40-48 |
|----------------------------|-------------------------------------|

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants achieving BCVA  $\geq$ 69 letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept.

|   |                                       |
|---|---------------------------------------|
| Comparison groups                       | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis | 593                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Parameter estimate                      | Difference in CMH Weighted Percentage |
| Point estimate                          | 5.7                                   |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -1.4                                  |
| upper limit                             | 12.9                                  |

### Secondary: Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA $\geq$ 69 Letters) in the Study Eye Over Time

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA $\geq$ 69 Letters) in the Study Eye Over Time |
|-----------------|--|

#### End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (<69 letters vs.  $\geq$ 69 letters), baseline LLD ( $\geq$ 33 letters and <33 letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[30]</sup> | 327 <sup>[31]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 45.7 (41.1 to 50.2) | 40.1 (35.8 to 44.5)   |  |  |
| Week 8 (n = 327, 322)             | 50.5 (45.8 to 55.1) | 45.2 (40.7 to 49.7)   |  |  |
| Week 12 (n = 326, 317)            | 53.5 (48.8 to 58.3) | 48.5 (43.8 to 53.3)   |  |  |
| Week 16 (n = 321, 315)            | 56.1 (51.2 to 60.9) | 47.4 (42.8 to 52.1)   |  |  |
| Week 20 (n = 320, 309)            | 57.5 (52.6 to 62.4) | 51.1 (46.3 to 55.9)   |  |  |
| Week 24 (n = 295, 288)            | 57.4 (52.4 to 62.4) | 47.8 (42.9 to 52.8)   |  |  |



|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 28 (n = 292, 271)  | 55.2 (50.0 to 60.4) | 48.2 (43.2 to 53.2) |  |  |
| Week 32 (n = 287, 288)  | 55.9 (50.8 to 61.1) | 49.8 (45.0 to 54.6) |  |  |
| Week 36 (n = 293, 283)  | 56.0 (50.9 to 61.0) | 47.4 (42.2 to 52.6) |  |  |
| Week 40 (n = 286, 288)  | 54.7 (49.5 to 59.9) | 52.7 (47.5 to 57.9) |  |  |
| Week 44 (n = 285, 273)  | 56.3 (51.4 to 61.3) | 52.5 (47.3 to 57.7) |  |  |
| Week 48 (n = 282, 277)  | 55.0 (49.8 to 60.2) | 52.3 (47.1 to 57.5) |  |  |
| Week 52 (n = 283, 273)  | 55.9 (50.6 to 61.1) | 55.6 (50.4 to 60.9) |  |  |
| Week 56 (n = 283, 273)  | 57.1 (51.8 to 62.3) | 52.9 (47.7 to 58.2) |  |  |
| Week 60 (n = 278, 273)  | 53.0 (47.6 to 58.3) | 53.6 (48.3 to 58.9) |  |  |
| Week 64 (n = 276, 266)  | 58.8 (53.5 to 64.2) | 52.9 (47.5 to 58.3) |  |  |
| Week 68 (n = 276, 266)  | 57.0 (51.7 to 62.4) | 55.5 (50.0 to 60.9) |  |  |
| Week 72 (n = 276, 261)  | 58.1 (52.7 to 63.4) | 53.3 (48.0 to 58.6) |  |  |
| Week 76 (n = 268, 267)  | 58.0 (52.6 to 63.4) | 54.0 (48.6 to 59.3) |  |  |
| Week 80 (n = 275, 264)  | 57.3 (52.0 to 62.6) | 51.9 (46.5 to 57.4) |  |  |
| Week 84 (n = 279, 254)  | 58.4 (53.1 to 63.7) | 56.9 (51.5 to 62.4) |  |  |
| Week 88 (n = 276, 253)  | 57.2 (51.9 to 62.6) | 51.1 (45.6 to 56.5) |  |  |
| Week 92 (n = 273, 253)  | 56.1 (50.8 to 61.4) | 54.9 (49.5 to 60.3) |  |  |
| Week 96 (n = 266, 247)  | 55.5 (49.9 to 61.0) | 53.9 (48.4 to 59.4) |  |  |
| Week 100 (n = 272, 254) | 55.1 (49.5 to 60.7) | 51.7 (46.2 to 57.2) |  |  |
| Week 104 (n = 263, 249) | 55.1 (49.4 to 60.7) | 52.8 (47.3 to 58.2) |  |  |
| Week 108 (n = 267, 247) | 54.8 (49.1 to 60.4) | 51.0 (45.5 to 56.5) |  |  |
| Week 112 (n = 267, 254) | 55.7 (50.2 to 61.1) | 51.0 (45.6 to 56.4) |  |  |

Notes:

[30] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[31] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA $\leq$ 38 Letters) in the Study Eye Averaged Over Weeks 40, 44, and 48

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA $\leq$ 38 Letters) in the Study Eye Averaged Over Weeks 40, 44, and 48 |
|-----------------|---|

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this

averaged value was used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.03% CI.

|   |           |
|---|-----------|
| End point type                            | Secondary |
| End point timeframe:                      |           |
| Baseline, average of Weeks 40, 44, and 48 |           |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 302 <sup>[32]</sup> | 291 <sup>[33]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  | 7.9 (5.0 to 10.8)   | 7.5 (4.7 to 10.3)     |  |  |

Notes:

[32] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

[33] - Participants with at least one non-missing, valid assessment at Weeks 40, 44, or 48.

## Statistical analyses

|                                   |                                     |
|-----------------------------------|-------------------------------------|
| <b>Statistical analysis title</b> | Treatment Difference at Weeks 40-48 |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants with BCVA  $\leq 38$  letters is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept.

|   |                                       |
|---|---------------------------------------|
| Comparison groups                       | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis | 593                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Parameter estimate                      | Difference in CMH Weighted Percentage |
| Point estimate                          | 0.4                                   |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -3.6                                  |
| upper limit                             | 4.4                                   |

## Secondary: Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA $\leq 38$ Letters) in the Study Eye Over Time

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA $\leq 38$ Letters) in the Study Eye Over Time |
|-----------------|--|

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$

letters), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.03% CI.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112 |           |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[34]</sup> | 327 <sup>[35]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 328, 323)             | 6.8 (4.3 to 9.4)    | 6.1 (3.7 to 8.5)      |  |  |
| Week 8 (n = 327, 322)             | 7.4 (4.8 to 10.1)   | 6.2 (3.7 to 8.6)      |  |  |
| Week 12 (n = 326, 317)            | 7.6 (5.0 to 10.2)   | 5.9 (3.5 to 8.3)      |  |  |
| Week 16 (n = 321, 315)            | 9.5 (6.6 to 12.5)   | 5.3 (3.0 to 7.6)      |  |  |
| Week 20 (n = 320, 309)            | 9.3 (6.4 to 12.3)   | 5.7 (3.3 to 8.1)      |  |  |
| Week 24 (n = 295, 288)            | 8.1 (5.2 to 11.1)   | 6.3 (3.7 to 8.9)      |  |  |
| Week 28 (n = 292, 271)            | 7.4 (4.6 to 10.3)   | 6.4 (3.7 to 9.1)      |  |  |
| Week 32 (n = 287, 288)            | 8.1 (5.1 to 11.0)   | 6.6 (4.0 to 9.2)      |  |  |
| Week 36 (n = 293, 283)            | 7.8 (4.9 to 10.6)   | 6.8 (4.1 to 9.5)      |  |  |
| Week 40 (n = 286, 288)            | 8.3 (5.3 to 11.3)   | 7.6 (4.8 to 10.3)     |  |  |
| Week 44 (n = 285, 273)            | 7.9 (4.9 to 10.9)   | 6.8 (4.0 to 9.5)      |  |  |
| Week 48 (n = 282, 277)            | 9.7 (6.5 to 12.9)   | 6.3 (3.6 to 9.0)      |  |  |
| Week 52 (n = 283, 273)            | 9.1 (6.0 to 12.2)   | 6.5 (3.7 to 9.2)      |  |  |
| Week 56 (n = 283, 273)            | 8.1 (5.1 to 11.1)   | 6.3 (3.6 to 9.0)      |  |  |
| Week 60 (n = 278, 273)            | 8.2 (5.2 to 11.3)   | 7.3 (4.5 to 10.2)     |  |  |
| Week 64 (n = 276, 266)            | 7.1 (4.2 to 10.1)   | 7.2 (4.3 to 10.1)     |  |  |
| Week 68 (n = 276, 266)            | 8.8 (5.6 to 12.0)   | 6.8 (4.0 to 9.6)      |  |  |
| Week 72 (n = 276, 261)            | 8.4 (5.2 to 11.6)   | 6.2 (3.4 to 8.9)      |  |  |
| Week 76 (n = 268, 267)            | 9.5 (6.2 to 12.9)   | 7.4 (4.5 to 10.3)     |  |  |
| Week 80 (n = 275, 264)            | 9.8 (6.5 to 13.1)   | 8.4 (5.3 to 11.5)     |  |  |
| Week 84 (n = 279, 254)            | 9.3 (6.0 to 12.6)   | 7.2 (4.2 to 10.1)     |  |  |

|                         |                    |                    |  |  |
|-------------------------|--------------------|--------------------|--|--|
| Week 88 (n = 276, 253)  | 8.4 (5.2 to 11.6)  | 7.5 (4.5 to 10.4)  |  |  |
| Week 92 (n = 273, 253)  | 8.9 (5.6 to 12.2)  | 9.0 (5.8 to 12.2)  |  |  |
| Week 96 (n = 266, 247)  | 10.4 (6.8 to 13.9) | 9.7 (6.5 to 13.0)  |  |  |
| Week 100 (n = 272, 254) | 10.3 (6.8 to 13.8) | 10.9 (7.5 to 14.4) |  |  |
| Week 104 (n = 263, 249) | 9.2 (5.8 to 12.6)  | 9.8 (6.4 to 13.1)  |  |  |
| Week 108 (n = 267, 247) | 9.5 (6.0 to 12.9)  | 10.0 (6.5 to 13.4) |  |  |
| Week 112 (n = 267, 254) | 9.0 (5.7 to 12.4)  | 10.6 (7.1 to 14.0) |  |  |

Notes:

[34] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[35] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants in the Faricimab Arm on Once Every 8-Weeks, 12-Weeks, or 16-Weeks Treatment Intervals Among Those Completing Week 48

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the Faricimab Arm on Once Every 8-Weeks, 12-Weeks, or 16-Weeks Treatment Intervals Among Those Completing Week 48 <sup>[36]</sup> |
|-----------------|---|

End point description:

Percentages are based on the number of participants randomized to the faricimab arm who have not discontinued the study at Week 48. The treatment interval at a given visit is defined as the treatment interval decision followed at that visit. The 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 48

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants who were randomized to Arm A: Faricimab.

| End point values                  | Arm A:<br>Faricimab |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 316                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| Once Every 8 Weeks                | 22.2 (17.6 to 26.7) |  |  |  |
| Once Every 12 Weeks               | 32.9 (27.7 to 38.1) |  |  |  |
| Once Every 16 Weeks               | 44.9 (39.4 to 50.4) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants in the Faricimab Arm on Once Every 8-Weeks, 12-Weeks, or 16-Weeks Treatment Intervals Among Those Completing Week 60

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants in the Faricimab Arm on Once Every 8-Weeks, 12-Weeks, or 16-Weeks Treatment Intervals Among Those Completing Week 60 <sup>[37]</sup> |
|-----------------|---|

#### End point description:

Percentages are based on the number of participants randomized to the faricimab arm who have not discontinued the study at Week 60. The treatment interval at a given visit is defined as the treatment interval decision followed at that visit. The 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

Week 60

#### Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants who were randomized to Arm A: Faricimab.

| End point values                  | Arm A:<br>Faricimab |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 305                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| Once Every 8 Weeks                | 21.6 (17.0 to 26.3) |  |  |  |
| Once Every 12 Weeks               | 32.8 (27.5 to 38.1) |  |  |  |
| Once Every 16 Weeks               | 45.6 (40.0 to 51.2) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants in the Faricimab Arm on Once Every 8-Weeks, 12-Weeks, or 16-Weeks Treatment Intervals Among Those Completing Week 112

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants in the Faricimab Arm on Once Every 8-Weeks, 12-Weeks, or 16-Weeks Treatment Intervals Among Those Completing Week 112 <sup>[38]</sup> |
|-----------------|--|

#### End point description:

Percentages are based on the number of participants randomized to the faricimab arm who have not discontinued the study at Week 112. Treatment interval at a given visit is defined as the treatment interval decision followed at that visit. Treatment interval at Week 112 is calculated using data recorded at Week 108. The 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

Weeks 108 and 112

#### Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants who were randomized to Arm A: Faricimab.

| End point values                  | Arm A:<br>Faricimab |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 287                 |  |  |  |
| Units: Percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  |                     |  |  |  |
| Once Every 8 Weeks                | 18.8 (14.3 to 23.3) |  |  |  |
| Once Every 12 Weeks               | 14.3 (10.2 to 18.3) |  |  |  |
| Once Every 16 Weeks               | 66.9 (61.4 to 72.4) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Study Drug Injections Received in the Study Eye Through Week 48

|                 |   |
|-----------------|---|
| End point title | Number of Study Drug Injections Received in the Study Eye Through Week 48 |
|-----------------|---|

End point description:

This analysis was performed on the safety-evaluable population, which included all participants who received at least one dose of active study drug (faricimab or aflibercept) in the study eye.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline through Week 48

| End point values              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-------------------------------|---------------------|-----------------------|--|--|
| Subject group type            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed   | 331                 | 326                   |  |  |
| Units: Injections             |                     |                       |  |  |
| median (full range (min-max)) | 6.0 (1 to 8)        | 8.0 (1 to 8)          |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Study Drug Injections Received in the Study Eye Through Week 60

|                 |   |
|-----------------|---|
| End point title | Number of Study Drug Injections Received in the Study Eye Through Week 60 |
|-----------------|---|

End point description:

This analysis was performed on the safety-evaluable population, which included all participants who received at least one dose of active study drug (faricimab or aflibercept) in the study eye.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline through Week 60

| End point values              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-------------------------------|---------------------|-----------------------|--|--|
| Subject group type            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed   | 331                 | 326                   |  |  |
| Units: Injections             |                     |                       |  |  |
| median (full range (min-max)) | 7.0 (1 to 10)       | 9.0 (1 to 9)          |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Study Drug Injections Received in the Study Eye Through Week 108

|                 |  |
|-----------------|--|
| End point title | Number of Study Drug Injections Received in the Study Eye Through Week 108 |
|-----------------|--|

End point description:

This analysis was performed on the safety-evaluable population, which included all participants who received at least one dose of active study drug (faricimab or aflibercept) in the study eye.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline through Week 108

| End point values              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-------------------------------|---------------------|-----------------------|--|--|
| Subject group type            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed   | 331                 | 326                   |  |  |
| Units: Injections             |                     |                       |  |  |
| median (full range (min-max)) | 10.0 (1 to 16)      | 15.0 (1 to 15)        |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Central Subfield Thickness in the Study Eye Averaged Over Weeks 40, 44, and 48

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Central Subfield Thickness in the |
|-----------------|---|

## End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE) using optical coherence tomography (OCT), as assessed by the central reading center. For the Mixed Model of Repeated Measures (MMRM) analysis, the model adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous), baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $< 33$  letters and  $\geq 33$  letters), and region (U.S. and Canada, Asia, and the rest of the world). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

From Baseline through Week 48

| End point values                          | Arm A:<br>Faricimab       | Arm B:<br>Aflibercept     |  |  |
|---|---------------------------|---------------------------|--|--|
| Subject group type                        | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed               | 331                       | 327                       |  |  |
| Units: microns                            |                           |                           |  |  |
| arithmetic mean (confidence interval 95%) | -137.1 (-143.1 to -131.2) | -130.8 (-136.8 to -124.8) |  |  |

## Statistical analyses

|                            |                                     |
|----------------------------|-------------------------------------|
| Statistical analysis title | Treatment Difference at Weeks 40-48 |
|----------------------------|-------------------------------------|

## Statistical analysis description:

The treatment difference in adjusted means of change from baseline CST is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. MMRM adjustments are listed in the outcome measure description.

|   |                                       |
|---|---------------------------------------|
| Comparison groups                       | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis | 658                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Parameter estimate                      | Adjusted mean difference              |
| Point estimate                          | -6.4                                  |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -14.8                                 |
| upper limit                             | 2.1                                   |
| Variability estimate                    | Standard error of the mean            |
| Dispersion value                        | 4.3                                   |

### Secondary: Change from Baseline in Central Subfield Thickness in the Study Eye Averaged Over Weeks 52, 56, and 60

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Central Subfield Thickness in the |
|-----------------|---|



## End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE) using optical coherence tomography (OCT), as assessed by the central reading center. For the Mixed Model of Repeated Measures (MMRM) analysis, the model adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous), baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $< 33$  letters and  $\geq 33$  letters), and region (U.S. and Canada, Asia, and the rest of the world). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

From Baseline through Week 60

| End point values                          | Arm A:<br>Faricimab       | Arm B:<br>Aflibercept     |  |  |
|---|---------------------------|---------------------------|--|--|
| Subject group type                        | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed               | 331                       | 327                       |  |  |
| Units: microns                            |                           |                           |  |  |
| arithmetic mean (confidence interval 95%) | -135.7 (-141.2 to -130.1) | -137.0 (-142.7 to -131.3) |  |  |

## Statistical analyses

|                            |                                     |
|----------------------------|-------------------------------------|
| Statistical analysis title | Treatment Difference at Weeks 52-60 |
|----------------------------|-------------------------------------|

## Statistical analysis description:

The treatment difference in adjusted means of change from baseline CST is the calculated difference of Arm A: Faricimab and Arm B: Aflibercept. MMRM adjustments are listed in the outcome measure description.

|   |                                       |
|---|---------------------------------------|
| Comparison groups                       | Arm A: Faricimab v Arm B: Aflibercept |
| Number of subjects included in analysis | 658                                   |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | other                                 |
| Parameter estimate                      | Adjusted mean difference              |
| Point estimate                          | 1.4                                   |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | -6.6                                  |
| upper limit                             | 9.3                                   |
| Variability estimate                    | Standard error of the mean            |
| Dispersion value                        | 4.05                                  |

## Secondary: Change from Baseline in Central Subfield Thickness in the Study Eye Over Time

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Central Subfield Thickness in the |
|-----------------|---|

## End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE) using optical coherence tomography (OCT), as assessed by the central reading center. For the Mixed Model of Repeated Measures (MMRM) analysis, the model adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous), baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $< 33$  letters and  $\geq 33$  letters), and region (U.S. and Canada, Asia, and the rest of the world). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, and 112

| End point values                          | Arm A:<br>Faricimab       | Arm B:<br>Aflibercept     |  |  |
|---|---------------------------|---------------------------|--|--|
| Subject group type                        | Reporting group           | Reporting group           |  |  |
| Number of subjects analysed               | 331                       | 327                       |  |  |
| Units: microns                            |                           |                           |  |  |
| arithmetic mean (confidence interval 95%) |                           |                           |  |  |
| Week 4                                    | -126.5 (-132.3 to -120.6) | -113.9 (-119.8 to -108.0) |  |  |
| Week 8                                    | -138.0 (-143.7 to -132.3) | -123.8 (-129.6 to -118.0) |  |  |
| Week 12                                   | -141.7 (-147.1 to -136.3) | -129.6 (-135.0 to -124.1) |  |  |
| Week 16                                   | -143.7 (-150.3 to -137.1) | -112.9 (-119.6 to -106.2) |  |  |
| Week 20                                   | -130.9 (-136.8 to -125.0) | -132.9 (-138.8 to -126.9) |  |  |
| Week 24                                   | -130.1 (-137.1 to -123.1) | -112.2 (-119.3 to -105.2) |  |  |
| Week 28                                   | -127.3 (-134.0 to -120.6) | -130.1 (-136.9 to -123.3) |  |  |
| Week 32                                   | -138.6 (-145.8 to -131.5) | -115.3 (-122.5 to -108.1) |  |  |
| Week 36                                   | -124.6 (-131.3 to -118.0) | -135.2 (-141.9 to -128.5) |  |  |
| Week 40                                   | -142.5 (-149.3 to -135.6) | -122.5 (-129.4 to -115.6) |  |  |
| Week 44                                   | -130.9 (-136.7 to -125.1) | -141.6 (-147.6 to -135.7) |  |  |
| Week 48                                   | -135.5 (-142.3 to -128.6) | -123.9 (-130.8 to -117.0) |  |  |
| Week 52                                   | -140.9 (-146.4 to -135.3) | -139.6 (-145.3 to -134.0) |  |  |
| Week 56                                   | -138.9 (-145.7 to -132.1) | -125.6 (-132.5 to -118.6) |  |  |
| Week 60                                   | -125.9 (-132.0 to -119.7) | -142.3 (-148.6 to -136.1) |  |  |
| Week 64                                   | -143.8 (-150.3 to -137.2) | -126.0 (-132.7 to -119.3) |  |  |
| Week 68                                   | -138.0 (-143.9 to -132.2) | -138.8 (-144.8 to -132.8) |  |  |

|          |                           |                           |  |  |
|----------|---------------------------|---------------------------|--|--|
| Week 72  | -140.7 (-147.3 to -134.1) | -128.8 (-135.5 to -122.0) |  |  |
| Week 76  | -136.1 (-142.4 to -129.7) | -139.0 (-145.4 to -132.6) |  |  |
| Week 80  | -144.4 (-151.1 to -137.8) | -128.7 (-135.5 to -121.9) |  |  |
| Week 84  | -143.5 (-149.2 to -137.8) | -143.2 (-149.1 to -137.4) |  |  |
| Week 88  | -145.5 (-151.6 to -139.5) | -133.3 (-139.5 to -127.1) |  |  |
| Week 92  | -142.1 (-148.0 to -136.1) | -143.2 (-149.3 to -137.1) |  |  |
| Week 96  | -146.8 (-153.1 to -140.4) | -134.7 (-141.2 to -128.2) |  |  |
| Week 100 | -145.0 (-151.7 to -138.3) | -146.2 (-153.1 to -139.3) |  |  |
| Week 104 | -149.6 (-156.3 to -142.8) | -137.4 (-144.3 to -130.5) |  |  |
| Week 108 | -148.5 (-154.4 to -142.6) | -148.3 (-154.4 to -142.2) |  |  |
| Week 112 | -152.9 (-159.2 to -146.7) | -139.1 (-145.5 to -132.7) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye Over Time

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye Over Time |
|-----------------|--|

End point description:

Intraretinal fluid was measured using optical coherence tomography (OCT) in the central subfield (center 1 millimetre [mm]). The weighted estimates of the percentage of participants with absence of intraretinal fluid were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world). Asia and rest of the world regions were combined due to a small number of enrolled participants. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[39]</sup> | 327 <sup>[40]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 324, 320)             | 86.9 (83.5 to 90.4) | 82.9 (78.9 to 87.0)   |  |  |

|                         |                     |                     |  |  |
|-------------------------|---------------------|---------------------|--|--|
| Week 8 (n = 324, 316)   | 88.5 (85.2 to 91.9) | 84.6 (80.7 to 88.5) |  |  |
| Week 12 (n = 323, 315)  | 87.5 (84.0 to 91.0) | 84.5 (80.6 to 88.5) |  |  |
| Week 16 (n = 320, 314)  | 90.6 (87.5 to 93.7) | 76.5 (71.9 to 81.0) |  |  |
| Week 20 (n = 320, 305)  | 78.8 (74.5 to 83.0) | 86.1 (82.3 to 89.8) |  |  |
| Week 24 (n = 294, 284)  | 78.7 (74.2 to 83.1) | 78.0 (73.4 to 82.7) |  |  |
| Week 28 (n = 291, 273)  | 77.1 (72.4 to 81.8) | 85.9 (81.8 to 89.9) |  |  |
| Week 32 (n = 286, 291)  | 86.3 (82.5 to 90.2) | 78.3 (73.6 to 82.9) |  |  |
| Week 36 (n = 293, 278)  | 79.6 (75.0 to 84.1) | 86.1 (82.1 to 90.1) |  |  |
| Week 40 (n = 277, 278)  | 84.5 (80.3 to 88.7) | 77.5 (72.7 to 82.3) |  |  |
| Week 44 (n = 275, 258)  | 78.5 (73.7 to 83.2) | 84.2 (79.9 to 88.5) |  |  |
| Week 48 (n = 274, 269)  | 84.1 (79.8 to 88.4) | 77.7 (72.8 to 82.5) |  |  |
| Week 52 (n = 281, 270)  | 85.9 (81.9 to 89.8) | 85.3 (81.1 to 89.4) |  |  |
| Week 56 (n = 281, 272)  | 85.2 (81.1 to 89.2) | 81.1 (76.6 to 85.6) |  |  |
| Week 60 (n = 273, 266)  | 77.8 (73.0 to 82.6) | 85.4 (81.2 to 89.5) |  |  |
| Week 104 (n = 259, 247) | 86.0 (81.9 to 90.1) | 80.0 (75.1 to 84.9) |  |  |
| Week 108 (n = 264, 243) | 82.2 (77.7 to 86.6) | 83.5 (79.0 to 88.1) |  |  |
| Week 112 (n = 266, 251) | 85.9 (81.8 to 90.0) | 80.5 (75.7 to 85.4) |  |  |

Notes:

[39] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[40] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with Absence of Subretinal Fluid in the Study Eye Over Time

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with Absence of Subretinal Fluid in the Study Eye Over Time |
|-----------------|--|

End point description:

Subretinal fluid was measured using optical coherence tomography (OCT) in the central subfield (center 1 mm). The weighted estimates of the percentage of participants with absence of subretinal fluid were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world). Asia and rest of the world regions were combined due to a small number of enrolled participants. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 104, 108, and 112

| <b>End point values</b>           | <b>Arm A:<br/>Faricimab</b> | <b>Arm B:<br/>Aflibercept</b> |  |  |
|-----------------------------------|-----------------------------|-------------------------------|--|--|
| Subject group type                | Reporting group             | Reporting group               |  |  |
| Number of subjects analysed       | 331 <sup>[41]</sup>         | 327 <sup>[42]</sup>           |  |  |
| Units: Percentage of participants |                             |                               |  |  |
| number (confidence interval 95%)  |                             |                               |  |  |
| Week 4 (n = 327, 319)             | 70.9 (66.1 to 75.7)         | 61.7 (56.4 to 66.9)           |  |  |
| Week 8 (n = 323, 319)             | 79.8 (75.6 to 84.1)         | 73.6 (68.9 to 78.4)           |  |  |
| Week 12 (n = 324, 315)            | 88.6 (85.1 to 92.0)         | 79.6 (75.3 to 84.0)           |  |  |
| Week 16 (n = 320, 315)            | 90.6 (87.4 to 93.8)         | 63.8 (58.6 to 68.9)           |  |  |
| Week 20 (n = 320, 308)            | 76.1 (71.6 to 80.7)         | 80.4 (76.1 to 84.8)           |  |  |
| Week 24 (n = 295, 287)            | 73.7 (68.8 to 78.5)         | 59.1 (53.5 to 64.6)           |  |  |
| Week 28 (n = 292, 272)            | 71.5 (66.6 to 76.4)         | 78.7 (73.9 to 83.5)           |  |  |
| Week 32 (n = 287, 291)            | 82.6 (78.3 to 87.0)         | 62.2 (56.7 to 67.7)           |  |  |
| Week 36 (n = 293, 282)            | 70.6 (65.5 to 75.7)         | 80.7 (76.1 to 85.2)           |  |  |
| Week 40 (n = 283, 285)            | 77.6 (72.9 to 82.3)         | 63.9 (58.4 to 69.5)           |  |  |
| Week 44 (n = 280, 269)            | 65.7 (60.3 to 71.0)         | 76.2 (71.1 to 81.2)           |  |  |
| Week 48 (n = 278, 274)            | 72.5 (67.5 to 77.5)         | 62.1 (56.5 to 67.7)           |  |  |
| Week 52 (n = 281, 271)            | 83.0 (78.8 to 87.3)         | 80.6 (76.0 to 85.3)           |  |  |
| Week 56 (n = 282, 271)            | 80.7 (76.3 to 85.2)         | 71.6 (66.4 to 76.8)           |  |  |
| Week 60 (n = 278, 271)            | 63.6 (58.1 to 69.0)         | 80.0 (75.3 to 84.8)           |  |  |
| Week 104 (n = 262, 248)           | 80.0 (75.3 to 84.7)         | 73.9 (68.5 to 79.3)           |  |  |
| Week 108 (n = 266, 244)           | 76.1 (71.2 to 81.0)         | 80.7 (75.8 to 85.5)           |  |  |
| Week 112 (n = 267, 252)           | 80.9 (76.4 to 85.4)         | 77.5 (72.4 to 82.6)           |  |  |

Notes:

[41] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[42] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with Absence of Intraretinal Fluid and Subretinal Fluid in the Study Eye Over Time

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with Absence of Intraretinal Fluid and Subretinal Fluid in the Study Eye Over Time |
|-----------------|---|

End point description:

Intraretinal fluid and subretinal fluid were measured using optical coherence tomography (OCT) in the central subfield (center 1 mm). The weighted estimates of the percentage of participants with absence of intraretinal and subretinal fluid were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$  letters, 73-55 letters, and  $\leq 54$  letters), baseline LLD ( $\geq 33$  letters and  $< 33$  letters), and region (U.S. and Canada vs. rest of the world). Asia and rest of the world regions were combined due to a small number of enrolled participants. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.03% CI.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 104, 108, and 112

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[43]</sup> | 327 <sup>[44]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 324, 319)             | 59.5 (54.2 to 64.8) | 49.8 (44.4 to 55.2)   |  |  |
| Week 8 (n = 323, 315)             | 70.2 (65.2 to 75.1) | 61.6 (56.3 to 66.9)   |  |  |
| Week 12 (n = 323, 315)            | 77.0 (72.4 to 81.5) | 66.6 (61.5 to 71.7)   |  |  |
| Week 16 (n = 319, 315)            | 82.4 (78.3 to 86.5) | 47.6 (42.2 to 53.0)   |  |  |
| Week 20 (n = 320, 305)            | 62.3 (57.3 to 67.4) | 68.6 (63.6 to 73.7)   |  |  |
| Week 24 (n = 295, 284)            | 56.5 (50.8 to 62.1) | 45.4 (39.7 to 51.1)   |  |  |
| Week 28 (n = 291, 273)            | 55.5 (49.9 to 61.1) | 66.5 (61.0 to 72.0)   |  |  |
| Week 32 (n = 286, 291)            | 73.1 (68.0 to 78.1) | 48.6 (42.9 to 54.3)   |  |  |
| Week 36 (n = 293, 278)            | 56.3 (50.8 to 61.9) | 68.3 (62.9 to 73.7)   |  |  |
| Week 40 (n = 278, 281)            | 65.8 (60.3 to 71.2) | 49.0 (43.2 to 54.8)   |  |  |
| Week 44 (n = 277, 262)            | 49.5 (43.7 to 55.3) | 64.3 (58.5 to 70.0)   |  |  |
| Week 48 (n = 277, 270)            | 62.2 (56.6 to 67.8) | 46.1 (40.3 to 52.0)   |  |  |
| Week 52 (n = 281, 270)            | 70.3 (65.2 to 75.5) | 68.8 (63.4 to 74.3)   |  |  |
| Week 56 (n = 281, 272)            | 66.9 (61.5 to 72.3) | 57.5 (51.8 to 63.3)   |  |  |
| Week 60 (n = 275, 266)            | 49.3 (43.5 to 55.0) | 69.1 (63.6 to 74.6)   |  |  |
| Week 104 (n = 259, 247)           | 68.1 (62.5 to 73.7) | 58.6 (52.7 to 64.6)   |  |  |
| Week 108 (n = 264, 243)           | 61.6 (55.9 to 67.3) | 67.1 (61.3 to 72.9)   |  |  |
| Week 112 (n = 266, 251)           | 68.7 (63.3 to 74.1) | 61.1 (55.1 to 67.1)   |  |  |

Notes:

[43] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[44] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with Absence of Pigment Epithelial Detachment in the Study Eye Over Time

|   |   |
|---|---|
| End point title   | Percentage of Participants with Absence of Pigment Epithelial Detachment in the Study Eye Over Time |
| End point description:  |   |
| Pigment epithelial detachment was measured using optical coherence tomography (OCT) in the central subfield (center 1 mm). The weighted estimates of the percentage of participants with absence of pigment epithelial detachment were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA ( $\geq 74$ letters, 73-55 letters, and $\leq 54$ letters), baseline LLD ( $\geq 33$ letters and $< 33$ letters), and region (U.S. and Canada vs. rest of the world). Asia and rest of the world regions were combined due to a small number of enrolled participants. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.03% CI. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Baseline, Weeks 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 104, 108, and 112   |   |

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 331 <sup>[45]</sup> | 327 <sup>[46]</sup>   |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  |                     |                       |  |  |
| Week 4 (n = 323, 320)             | 3.7 (1.7 to 5.8)    | 5.6 (3.1 to 8.1)      |  |  |
| Week 8 (n = 321, 318)             | 3.1 (1.3 to 5.0)    | 4.1 (1.9 to 6.2)      |  |  |
| Week 12 (n = 321, 314)            | 4.7 (2.4 to 7.0)    | 5.5 (3.0 to 8.0)      |  |  |
| Week 16 (n = 316, 313)            | 2.5 (0.8 to 4.1)    | 5.8 (3.2 to 8.4)      |  |  |
| Week 20 (n = 316, 306)            | 3.8 (1.7 to 5.9)    | 6.0 (3.4 to 8.6)      |  |  |
| Week 24 (n = 293, 284)            | 4.1 (1.8 to 6.3)    | 4.9 (2.5 to 7.4)      |  |  |
| Week 28 (n = 292, 273)            | 2.6 (0.9 to 4.4)    | 1.9 (0.3 to 3.5)      |  |  |
| Week 32 (n = 287, 291)            | 4.3 (2.0 to 6.6)    | 1.8 (0.3 to 3.3)      |  |  |
| Week 36 (n = 293, 283)            | 4.8 (2.4 to 7.1)    | 3.9 (1.7 to 6.1)      |  |  |
| Week 40 (n = 284, 286)            | 6.3 (3.5 to 9.0)    | 7.3 (4.4 to 10.3)     |  |  |
| Week 44 (n = 282, 270)            | 3.9 (1.7 to 6.2)    | 9.1 (5.9 to 12.4)     |  |  |
| Week 48 (n = 280, 275)            | 3.3 (1.2 to 5.3)    | 6.5 (3.7 to 9.3)      |  |  |
| Week 52 (n = 273, 267)            | 5.8 (3.1 to 8.5)    | 8.1 (5.0 to 11.3)     |  |  |
| Week 56 (n = 272, 266)            | 4.7 (2.3 to 7.2)    | 5.2 (2.7 to 7.7)      |  |  |
| Week 60 (n = 278, 271)            | 3.5 (1.4 to 5.6)    | 6.3 (3.4 to 9.1)      |  |  |

|                         |                   |                    |  |  |
|-------------------------|-------------------|--------------------|--|--|
| Week 104 (n = 260, 246) | 8.0 (4.8 to 11.2) | 8.3 (5.0 to 11.7)  |  |  |
| Week 108 (n = 264, 244) | 6.9 (3.9 to 10.0) | 8.0 (4.7 to 11.2)  |  |  |
| Week 112 (n = 264, 248) | 8.1 (4.9 to 11.3) | 12.5 (8.4 to 16.5) |  |  |

Notes:

[45] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

[46] - The 'n' analyzed indicates subjects with a non-missing, valid assessment at a given timepoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with Absence of Intraretinal Cysts in the Study Eye Over Time

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with Absence of Intraretinal Cysts in the Study Eye Over Time |
|-----------------|--|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 112 weeks

| End point values                  | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|-----------------------------------|---------------------|-----------------------|--|--|
| Subject group type                | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed       | 0 <sup>[47]</sup>   | 0 <sup>[48]</sup>     |  |  |
| Units: Percentage of participants |                     |                       |  |  |
| number (confidence interval 95%)  | ( to )              | ( to )                |  |  |

Notes:

[47] - Not evaluated; absence of intraretinal (IR) fluid and IR cysts are described by the same variable.

[48] - Not evaluated; absence of intraretinal (IR) fluid and IR cysts are described by the same variable.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Total Area of Choroidal Neovascularization Lesion in the Study Eye at Week 48

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Total Area of Choroidal Neovascularization Lesion in the Study Eye at Week 48 |
|-----------------|---|

End point description:

The total area of the choroidal neovascularization lesion in the study eye was evaluated by a central reading center using fundus fluorescein angiography (FFA). Assessments were censored following COVID-19 related intercurrent events. Baseline was defined as the last available measurement obtained on or prior to randomization.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Week 48



| End point values                              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed                   | 240                 | 236                   |  |  |
| Units: millimetres squared (mm <sup>2</sup> ) |                     |                       |  |  |
| arithmetic mean (standard deviation)          | 0.3 (± 4.6)         | 1.1 (± 4.4)           |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Total Area of Choroidal Neovascularization Lesion in the Study Eye at Week 112

|  |  |
|--|--|
| End point title  | Change from Baseline in Total Area of Choroidal Neovascularization Lesion in the Study Eye at Week 112 |
| End point description:<br>The total area of the choroidal neovascularization lesion in the study eye was evaluated by a central reading center using fundus fluorescein angiography (FFA). Assessments were censored following COVID-19 related intercurrent events. Baseline was defined as the last available measurement obtained on or prior to randomization. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Baseline and Week 112  |  |

| End point values                              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed                   | 240                 | 224                   |  |  |
| Units: millimetres squared (mm <sup>2</sup> ) |                     |                       |  |  |
| arithmetic mean (standard deviation)          | 1.7 (± 7.5)         | 1.7 (± 4.2)           |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Total Area of Choroidal Neovascularization Leakage in the Study Eye at Week 48

|   |  |
|---|--|
| End point title   | Change from Baseline in Total Area of Choroidal Neovascularization Leakage in the Study Eye at Week 48 |
| End point description:<br>The total area of choroidal neovascularization leakage in the study eye was evaluated by a central reading center using fundus fluorescein angiography (FFA). Assessments were censored following COVID-19 related intercurrent events. Baseline was defined as the last available measurement obtained |  |

on or prior to randomization.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and Week 48 |           |

| End point values                              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed                   | 241                 | 238                   |  |  |
| Units: millimetres squared (mm <sup>2</sup> ) |                     |                       |  |  |
| arithmetic mean (standard deviation)          | -3.3 (± 6.6)        | -2.1 (± 6.3)          |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Total Area of Choroidal Neovascularization Leakage in the Study Eye at Week 112

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Total Area of Choroidal Neovascularization Leakage in the Study Eye at Week 112 |
|-----------------|---|

End point description:

The total area of choroidal neovascularization leakage in the study eye was evaluated by a central reading center using fundus fluorescein angiography (FFA). Assessments were censored following COVID-19 related intercurrent events. Baseline was defined as the last available measurement obtained on or prior to randomization.

|                       |           |
|-----------------------|-----------|
| End point type        | Secondary |
| End point timeframe:  |           |
| Baseline and Week 112 |           |

| End point values                              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed                   | 239                 | 220                   |  |  |
| Units: millimetres squared (mm <sup>2</sup> ) |                     |                       |  |  |
| arithmetic mean (standard deviation)          | -5.3 (± 7.2)        | -4.2 (± 5.9)          |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with at Least One Adverse Event

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with at Least One Adverse Event |
|-----------------|--|

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**End point description:**

This analysis of adverse events (AEs) includes both ocular and non-ocular (systemic) AEs and is conducted on the safety-evaluable population. Multiple occurrences of the same AE in one individual are counted only once. Investigators sought information on AEs at each contact with the participants. All AEs were recorded and the investigator made an assessment of seriousness, severity, and causality of each AE. AEs of special interest included the following: Cases of potential drug-induced liver injury that include an elevated ALT or AST in combination with either an elevated bilirubin or clinical jaundice, as defined by Hy's Law; Suspected transmission of an infectious agent by the study drug; Sight-threatening AEs that cause a drop in visual acuity (VA) score  $\geq 30$  letters lasting more than 1 hour, require surgical or medical intervention to prevent permanent loss of sight, or are associated with severe intraocular inflammation (IOI).

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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**End point timeframe:**

From first dose of study drug through end of study (up to 112 weeks)

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| End point values                              | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|---|---------------------|-----------------------|--|--|
| Subject group type                            | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed                   | 331                 | 326                   |  |  |
| Units: Percentage of participants             |                     |                       |  |  |
| number (not applicable)                       |                     |                       |  |  |
| Adverse Event (AE)                            | 84.9                | 88.0                  |  |  |
| Serious AE (SAE)                              | 27.5                | 31.0                  |  |  |
| AE Leading to Withdrawal from Study Treatment | 4.8                 | 2.8                   |  |  |
| AE of Special Interest (AESI)                 | 7.3                 | 6.1                   |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Percentage of Participants with at Least One Ocular Adverse Event in the Study Eye or the Fellow Eye**

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|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with at Least One Ocular Adverse Event in the Study Eye or the Fellow Eye |
|-----------------|--|

---

**End point description:**

This analysis of adverse events (AEs) is conducted on the safety-evaluable population, which includes all participants who received at least one dose of active study drug (faricimab or aflibercept) in the study eye. It only includes ocular AEs, which are categorized as having occurred either in the study eye or the fellow eye. Multiple occurrences of the same AE in one individual are counted only once. Investigators sought information on AEs at each contact with the participants. All AEs were recorded and the investigator made an assessment of seriousness, severity, and causality of each AE. Ocular AEs of special interest included the following: Suspected transmission of an infectious agent by the study drug; Sight-threatening AEs that cause a drop in visual acuity (VA) score  $\geq 30$  letters lasting more than 1 hour, require surgical or medical intervention to prevent permanent loss of sight, or are associated with severe intraocular inflammation (IOI).

---

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

---

**End point timeframe:**

From first dose of study drug through end of study (up to 112 weeks)

---

| End point values                                     | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|--|---------------------|-----------------------|--|--|
| Subject group type                                   | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed                          | 331                 | 326                   |  |  |
| Units: Percentage of participants                    |                     |                       |  |  |
| number (not applicable)                              |                     |                       |  |  |
| Study Eye: Adverse Event (AE)                        | 52.9                | 47.5                  |  |  |
| Study Eye: Serious AE (SAE)                          | 4.5                 | 4.9                   |  |  |
| Study Eye: AE Leading to Withdrawal from Treatment   | 3.3                 | 1.8                   |  |  |
| Study Eye: Treatment-related AE                      | 3.6                 | 3.1                   |  |  |
| Study Eye: Treatment-related SAE                     | 1.8                 | 0.6                   |  |  |
| Study Eye: AE of Special Interest (AESI)             | 3.9                 | 4.3                   |  |  |
| Study Eye: AESI, Drop in VA Score $\geq 30$ Letters  | 2.7                 | 3.1                   |  |  |
| Study Eye: AESI, Associated with Severe IOI          | 0.6                 | 0.3                   |  |  |
| StudyEye:AESI,Interv Req to Avoid Perm Vision Loss   | 0.6                 | 0.9                   |  |  |
| StudyEye:Suspected Transm Infectious Agent by Drug   | 0.0                 | 0.3                   |  |  |
| Fellow Eye: AE                                       | 46.2                | 41.7                  |  |  |
| Fellow Eye: SAE                                      | 3.6                 | 2.5                   |  |  |
| Fellow Eye: AESI                                     | 3.0                 | 2.1                   |  |  |
| Fellow Eye: AESI, Drop in VA Score $\geq 30$ Letters | 2.1                 | 1.8                   |  |  |
| FellowEye:AESI,Inter Req to Avoid Perm Vision Loss   | 0.9                 | 0.3                   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with at Least One Non-Ocular Adverse Event

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with at Least One Non-Ocular Adverse Event |
|-----------------|---|

End point description:

This analysis of adverse events (AEs) is conducted on the safety-evaluable population, which includes all participants who received at least one dose of active study drug (faricimab or aflibercept) in the study eye. It only includes non-ocular (systemic) AEs. Multiple occurrences of the same AE in one individual are counted only once. Investigators sought information on AEs at each contact with the participants. All AEs were recorded and the investigator made an assessment of seriousness, severity, and causality of each AE. The non-ocular AE of special interest was: Cases of potential drug-induced liver injury that include an elevated ALT or AST in combination with either an elevated bilirubin or clinical jaundice, as defined by Hy's Law.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose of study drug through end of study (up to 112 weeks)

| End point values                                 | Arm A:<br>Faricimab | Arm B:<br>Aflibercept |  |  |
|--|---------------------|-----------------------|--|--|
| Subject group type                               | Reporting group     | Reporting group       |  |  |
| Number of subjects analysed                      | 331                 | 326                   |  |  |
| Units: Percentage of participants                |                     |                       |  |  |
| number (not applicable)                          |                     |                       |  |  |
| Adverse Event (AE)                               | 71.0                | 75.8                  |  |  |
| Serious AE (SAE)                                 | 21.8                | 26.4                  |  |  |
| AE Leading to Withdrawal from Study<br>Treatment | 1.5                 | 0.9                   |  |  |
| AE of Special Interest (AESI)                    | 0.3                 | 0.0                   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Concentration of Faricimab Over Time

|                 |   |
|-----------------|---|
| End point title | Plasma Concentration of Faricimab Over Time <sup>[49]</sup> |
|-----------------|---|

End point description:

Faricimab concentration in plasma was determined using a validated immunoassay method. This analysis only includes Arm A participants who received treatment with faricimab in the pharmacokinetic-evaluable population, which includes all safety-evaluable participants with at least one plasma sample, provided sufficient dosing information (dose and dosing time) was available. The number of participants analyzed at a given timepoint includes those with an available plasma sample and dosing information at that timepoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre-dose at Baseline, Weeks 4, 16, 20, 48, 76, and 112

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants who were randomized to Arm A: Faricimab.

| End point values                         | Arm A:<br>Faricimab |  |  |  |
|--|---------------------|--|--|--|
| Subject group type                       | Reporting group     |  |  |  |
| Number of subjects analysed              | 331                 |  |  |  |
| Units: micrograms per millilitre (µg/mL) |                     |  |  |  |
| arithmetic mean (standard deviation)     |                     |  |  |  |
| Baseline (n = 321)                       | 0.0000 (± 0.0001)   |  |  |  |
| Week 4 (n = 319)                         | 0.0287 (± 0.0209)   |  |  |  |
| Week 16 (n = 300)                        | 0.0333 (± 0.0250)   |  |  |  |
| Week 20 (n = 305)                        | 0.0046 (± 0.0051)   |  |  |  |
| Week 48 (n = 273)                        | 0.0149 (± 0.0185)   |  |  |  |
| Week 76 (n = 269)                        | 0.0053 (± 0.0117)   |  |  |  |
| Week 112 (n = 278)                       | 0.0119 (± 0.0149)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants who Tested Positive for Treatment-Emergent Anti-Drug Antibodies Against Faricimab During the Study

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Tested Positive for Treatment-Emergent Anti-Drug Antibodies Against Faricimab During the Study <sup>[50]</sup> |
|-----------------|---|

#### End point description:

Anti-drug antibodies (ADAs) against faricimab were detected in plasma using a validated bridging enzyme-linked immunosorbent assay (ELISA). The percentage of participants with treatment-emergent ADA-positive samples includes post-baseline evaluable participants with at least one treatment-induced (defined as having an ADA-negative sample or missing sample at baseline and any positive post-baseline sample) or treatment-boosted (defined as having an ADA-positive sample at baseline and any positive post-baseline sample with a titer that is equal to or greater than 4-fold baseline titer) ADA-positive sample during the study treatment period. The immunogenicity-analysis population includes all participants randomized to the faricimab arm with at least one determinant ADA assessment. Only those with at least one post-baseline ADA assessment were included in this analysis.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

Pre-dose at Baseline, Weeks 4, 20, 48, 76, and 112

#### Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only applicable to participants who were randomized to Arm A: Faricimab.

| End point values                      | Arm A:<br>Faricimab |  |  |  |
|---------------------------------------|---------------------|--|--|--|
| Subject group type                    | Reporting group     |  |  |  |
| Number of subjects analysed           | 330                 |  |  |  |
| Units: Percentage of participants     |                     |  |  |  |
| number (not applicable)               |                     |  |  |  |
| Total Treatment-Emergent ADA-Positive | 16.1                |  |  |  |
| Treatment-Induced ADA-Positive        | 16.1                |  |  |  |
| Treatment-Boosted ADA-Positive        | 0.0                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through end of study (up to 112 weeks)

Adverse event reporting additional description:

Adverse events (AEs) are reported for the safety population, which includes all participants who received at least one injection of active study drug (faricimab or aflibercept) in the study eye. For ocular AEs, the number of participants and events reported per term are combined totals of AEs that occurred in the study eye or the fellow eye.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Arm B: Aflibercept |
|-----------------------|--------------------|

Reporting group description:

Subjects randomized to the active comparator (Arm B) received a 2-mg dose of aflibercept that was administered intravitreally (IVT) Q8W, after 3 consecutive monthly doses during the 108-week treatment period. Subjects were to receive 15 IVT injections of aflibercept during the 108-week treatment period comprising three initiating injections (2 mg of aflibercept Q4W to Week 8), followed by 12 maintenance injections (2 mg of aflibercept Q8W at Weeks 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, and 104).

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Arm A: Faricimab |
|-----------------------|------------------|

Reporting group description:

Subjects randomized to Arm A received 6 mg of faricimab intravitreally (IVT) once every 4 weeks (Q4W) up to Week 12 (4 injections). At Week 20, protocol-defined assessment of disease activity required Arm A subjects with active disease to be treated with a once every 8 weeks (Q8W) dosing regimen of 6 mg of faricimab (i.e., at Weeks 20, 28, 36, 44, 52, and 60). A second assessment of disease activity at Week 24 required Arm A subjects with active disease (excluding those with active disease at Week 20) to be treated with a once every 12 weeks (Q12W) dosing regimen of 6 mg of faricimab IVT (i.e., at Weeks 24, 36, 48, and 60). Subjects who did not have active disease at Weeks 20 and 24 were treated with 6 mg of faricimab IVT once every 16 weeks (Q16W; i.e., at Weeks 28, 44, and 60). From Week 60 (when all of Arm A was scheduled to receive study drug) to Week 108, Arm A subjects were to be treated according to a personalized treatment interval (PTI) dosing regimen (Q8W, Q12W, or Q16W).

| Serious adverse events  | Arm B: Aflibercept | Arm A: Faricimab  |  |
|---|--------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                    |                   |  |
| subjects affected / exposed   | 101 / 326 (30.98%) | 91 / 331 (27.49%) |  |
| number of deaths (all causes)                                       | 14                 | 10                |  |
| number of deaths resulting from adverse events                      | 0                  | 0                 |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                   |  |
| Colon adenoma   |                    |                   |  |
| subjects affected / exposed   | 1 / 326 (0.31%)    | 0 / 331 (0.00%)   |  |
| occurrences causally related to treatment / all                     | 0 / 1              | 0 / 0             |  |
| deaths causally related to treatment / all                          | 0 / 0              | 0 / 0             |  |
| Bladder neoplasm  |                    |                   |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Bile duct cancer                                     |                 |                 |  |
| subjects affected / exposed                          | 2 / 326 (0.61%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Extranodal marginal zone B-cell lymphoma (MALT type) |                 |                 |  |
| subjects affected / exposed                          | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Lung neoplasm malignant                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 326 (0.00%) | 3 / 331 (0.91%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 3           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           |  |
| Lung cancer metastatic                               |                 |                 |  |
| subjects affected / exposed                          | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Glioblastoma multiforme                              |                 |                 |  |
| subjects affected / exposed                          | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Metastases to liver                                  |                 |                 |  |
| subjects affected / exposed                          | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Ovarian cancer metastatic                            |                 |                 |  |
| subjects affected / exposed                          | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Pancreatic carcinoma                                 |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Sarcomatoid carcinoma                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sarcomatoid carcinoma of the lung               |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Basal cell carcinoma                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatic neoplasm                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Colon cancer stage IV                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Cerebral haemangioma                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin cancer                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bladder cancer                                  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lung adenocarcinoma                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Breast cancer                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neoplasm  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Adenocarcinoma of colon                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Prostate cancer                                 |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tongue neoplasm malignant stage unspecified     |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vascular disorders                              |                 |                 |  |
| Hypertension                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Orthostatic hypotension                         |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Peripheral arterial occlusive disease                |                 |                 |  |
| subjects affected / exposed                          | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Venous thrombosis limb                               |                 |                 |  |
| subjects affected / exposed                          | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Deep vein thrombosis                                 |                 |                 |  |
| subjects affected / exposed                          | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Haematoma  |                 |                 |  |
| subjects affected / exposed                          | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Peripheral ischaemia                                 |                 |                 |  |
| subjects affected / exposed                          | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| 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 |                 |                 |  |
| Adverse drug reaction                                |                 |                 |  |
| subjects affected / exposed                          | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Death  |                 |                 |  |
| subjects affected / exposed                          | 2 / 326 (0.61%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 2           | 0 / 2           |  |
| Pain   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ill-defined disorder                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Asthenia  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Chest pain                                      |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Reproductive system and breast disorders        |                 |                 |  |
| Prostatomegaly                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Prostatic disorder                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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 |                 |                 |  |
| Bronchiectasis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Asthma  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Chronic obstructive pulmonary disease           |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 3 / 331 (0.91%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dyspnoea  |                 |                 |  |
| subjects affected / exposed                     | 4 / 326 (1.23%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypoxia   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Interstitial lung disease                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lung perforation                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Pneumonitis                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Haemothorax                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary artery thrombosis                     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory distress                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute respiratory failure                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Epistaxis                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| 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                     | 3 / 326 (0.92%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |
| Mixed anxiety and depressive disorder           |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Anxiety   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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 malfunction                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Investigations                                  |                 |                 |  |
| Intraocular pressure increased                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Weight decreased                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications  |                 |                 |  |
| Facial bones fracture                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Asbestosis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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                     | 3 / 326 (0.92%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Hip fracture                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Joint dislocation                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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                     | 1 / 326 (0.31%) | 0 / 331 (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                     | 2 / 326 (0.61%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper limb fracture                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Alcohol poisoning                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cataract operation complication                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Comminuted fracture                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Head injury                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Foot fracture                                   |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hyphaema  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cataract traumatic                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Humerus fracture                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal anastomotic leak               |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Acute myocardial infarction                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Angina pectoris                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 1 / 4           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrial fibrillation                             |                 |                 |  |
| subjects affected / exposed                     | 3 / 326 (0.92%) | 3 / 331 (0.91%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac failure                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 3 / 326 (0.92%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 1 / 2           |  |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 1           |  |
| Cardiac failure congestive                      |                 |                 |  |
| subjects affected / exposed                     | 6 / 326 (1.84%) | 3 / 331 (0.91%) |  |
| occurrences causally related to treatment / all | 0 / 11          | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiopulmonary failure                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Congestive cardiomyopathy                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Coronary artery disease                         |                 |                 |  |
| subjects affected / exposed                     | 3 / 326 (0.92%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dressler's syndrome                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myocardial infarction                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Paroxysmal atrioventricular block               |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pericardial effusion                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pericarditis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ventricular extrasystoles                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ventricular fibrillation                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac failure chronic                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Coronary artery occlusion                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Brain oedema                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Cerebral haemorrhage                            |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cerebrovascular accident                        |                 |                 |  |
| subjects affected / exposed                     | 5 / 326 (1.53%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 9           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ischaemic stroke                                |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Presyncope                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Postictal paralysis                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Syncope   |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Subarachnoid haemorrhage                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Seizure   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Thrombotic cerebral infarction                  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Transient ischaemic attack                      |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vascular dementia                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Quadriplegia                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dementia  |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dementia Alzheimer's type                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ischaemic cerebral infarction                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |
| Anaemia   |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Iron deficiency anaemia                         |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancytopenia                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Febrile neutropenia                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ear and labyrinth disorders                     |                 |                 |  |
| Vertigo   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Eye disorders                                   |                 |                 |  |
| Angle closure glaucoma                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cataract  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Corneal oedema                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Eye allergy                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Macular degeneration                            |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neovascular age-related macular degeneration    |                 |                 |  |
| subjects affected / exposed                     | 4 / 326 (1.23%) | 8 / 331 (2.42%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 8           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Retinal haemorrhage                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Retinal pigment epithelial tear                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 2 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Retinal vein occlusion                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vitreous haemorrhage                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 3 / 331 (0.91%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Uveitis   |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 1 / 2           | 2 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vitritis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Non-infectious endophthalmitis                  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                         | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all     | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Visual acuity reduced                               |                 |                 |  |
| subjects affected / exposed                         | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Retinal tear  |                 |                 |  |
| subjects affected / exposed                         | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Age-related macular degeneration                    |                 |                 |  |
| subjects affected / exposed                         | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Peripheral exudative haemorrhagic chorioretinopathy |                 |                 |  |
| subjects affected / exposed                         | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Diplopia  |                 |                 |  |
| subjects affected / exposed                         | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Dry age-related macular degeneration                |                 |                 |  |
| subjects affected / exposed                         | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Corneal opacity                                     |                 |                 |  |
| subjects affected / exposed                         | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                          |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Abdominal pain                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ascites   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Constipation                                    |                 |                 |  |
| subjects affected / exposed                     | 3 / 326 (0.92%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diarrhoea                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastritis                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diverticulum intestinal                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal haemorrhage                    |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper gastrointestinal haemorrhage              |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oesophagitis                                    |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastric dysplasia                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Intestinal obstruction                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Abdominal pain upper                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oesophageal ulcer                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Food poisoning                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Large intestine perforation                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lower gastrointestinal haemorrhage              |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Inguinal hernia                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Biliary obstruction                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholecystitis acute                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholecystitis                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholangitis acute                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Cystitis haemorrhagic                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Acute kidney injury                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal colic                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| 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                                       |                 |                 |  |
| Arthritis                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Fracture nonunion                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| 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                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Muscular weakness                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal stiffness                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (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                     | 2 / 326 (0.61%) | 4 / 331 (1.21%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 4           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rhabdomyolysis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Spondylolisthesis                               |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rheumatic disorder                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| COVID-19  |                 |                 |  |
| subjects affected / exposed                     | 4 / 326 (1.23%) | 3 / 331 (0.91%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis                                      |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Chorioretinitis                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diverticulitis                                  |                 |                 |  |
| subjects affected / exposed                     | 2 / 326 (0.61%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Endophthalmitis                                 |                 |                 |  |
| subjects affected / exposed                     | 3 / 326 (0.92%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 1 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infectious pleural effusion                     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                                   | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                    | 0 / 0           | 0 / 0           |  |
| Influenza   |                 |                 |  |
| subjects affected / exposed                                   | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                    | 0 / 0           | 0 / 0           |  |
| Infective exacerbation of chronic obstructive airways disease |                 |                 |  |
| subjects affected / exposed                                   | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all                    | 0 / 0           | 0 / 0           |  |
| Necrotising fasciitis   |                 |                 |  |
| subjects affected / exposed                                   | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all                    | 0 / 0           | 0 / 0           |  |
| Osteomyelitis   |                 |                 |  |
| subjects affected / exposed                                   | 1 / 326 (0.31%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all               | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all                    | 0 / 0           | 0 / 0           |  |
| Pneumonia   |                 |                 |  |
| subjects affected / exposed                                   | 6 / 326 (1.84%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all               | 0 / 7           | 0 / 2           |  |
| deaths causally related to treatment / all                    | 0 / 0           | 0 / 0           |  |
| Pyelonephritis acute  |                 |                 |  |
| subjects affected / exposed                                   | 1 / 326 (0.31%) | 0 / 331 (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                                   | 5 / 326 (1.53%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 5           | 0 / 0           |  |
| deaths causally related to treatment / all                    | 0 / 0           | 0 / 0           |  |
| Viral uveitis   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 326 (0.00%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Clostridium difficile colitis                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| COVID-19 pneumonia                              |                 |                 |  |
| subjects affected / exposed                     | 7 / 326 (2.15%) | 2 / 331 (0.60%) |  |
| occurrences causally related to treatment / all | 0 / 7           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 0           |  |
| Endocarditis                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 326 (0.00%) | 1 / 331 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vestibular neuronitis                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Hyperkalaemia                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypokalaemia                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vitamin B12 deficiency                          |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hyponatraemia                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gout  |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypervolaemia                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Type 2 diabetes mellitus                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 326 (0.31%) | 0 / 331 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Arm B: Aflibercept | Arm A: Faricimab   |  |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                    |                    |  |
| subjects affected / exposed                           | 165 / 326 (50.61%) | 178 / 331 (53.78%) |  |
| Injury, poisoning and procedural complications        |                    |                    |  |
| Fall  |                    |                    |  |
| subjects affected / exposed                           | 22 / 326 (6.75%)   | 18 / 331 (5.44%)   |  |
| occurrences (all)                                     | 27                 | 20                 |  |
| Vascular disorders                                    |                    |                    |  |
| Hypertension  |                    |                    |  |
| subjects affected / exposed                           | 18 / 326 (5.52%)   | 15 / 331 (4.53%)   |  |
| occurrences (all)                                     | 18                 | 15                 |  |
| Eye disorders   |                    |                    |  |



|   |                         |                          |  |
|---|-------------------------|--------------------------|--|
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)                        | 37 / 326 (11.35%)<br>72 | 35 / 331 (10.57%)<br>47  |  |
| Neovascular age-related macular<br>degeneration<br>subjects affected / exposed<br>occurrences (all) | 62 / 326 (19.02%)<br>81 | 80 / 331 (24.17%)<br>103 |  |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)   | 21 / 326 (6.44%)<br>37  | 15 / 331 (4.53%)<br>27   |  |
| Cataract<br>subjects affected / exposed<br>occurrences (all)  | 26 / 326 (7.98%)<br>38  | 38 / 331 (11.48%)<br>55  |  |
| Vitreous detachment<br>subjects affected / exposed<br>occurrences (all)                             | 21 / 326 (6.44%)<br>26  | 22 / 331 (6.65%)<br>29   |  |
| Posterior capsule opacification<br>subjects affected / exposed<br>occurrences (all)                 | 19 / 326 (5.83%)<br>23  | 15 / 331 (4.53%)<br>20   |  |
| Infections and infestations   |                         |                          |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                                 | 22 / 326 (6.75%)<br>25  | 27 / 331 (8.16%)<br>33   |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                         | 29 / 326 (8.90%)<br>36  | 19 / 331 (5.74%)<br>23   |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 28 February 2019 | Protocol Version 2: Amended to address feedback from the Voluntary Harmonisation Procedure. To enhance patient safety and to comply with health authority requests, patients with a known hypersensitivity to fluorescein were excluded. Also, the criterion for interruption and resuming study treatment after IOI was amended for clarity.  |
| 06 August 2019   | Protocol Version 3: -The criteria for the extension of the drug-dosing interval during the PTI phase was changed from a qualitative assessment of the presence of fluid to a quantitative assessment of CST stability.; -The study-eye inclusion criteria were amended to include patients with extrafoveal CNV membranes with a subfoveal component, secondary to nAMD.; -To ensure appropriate patient representation, the Sponsor could elect to cap the recruitment of patients in certain baseline BCVA strata.; -Reporting of medication errors and associated AE was updated. Medication errors were no longer to be reported expeditiously (within 24 hours), unless they caused a SAE or AESI. -As applicable throughout the protocol, the term "free" was added before VEGF-A and Ang-2 to more accurately describe what the assays were measuring and to be consistent with the other sections of the protocol. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported