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 (TENAYA)

Summary

EudraCT number	2018-002152-32
Trial protocol	DE HU GB PL ES NL IT
Global end of trial date	18 January 2022

Results information

Result version number	v1 (current)
This version publication date	01 February 2023
First version publication date	01 February 2023

Trial information

Trial identification

Sponsor protocol code	GR40306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03823287
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche, Ltd.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
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	18 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 October 2020
Global end of trial reached?	Yes
Global end of trial date	18 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	19 February 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	Canada: 34
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Israel: 30
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Japan: 52
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 48
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	Turkey: 10
Country: Number of subjects enrolled	United Kingdom: 59
Country: Number of subjects enrolled	United States: 332
Worldwide total number of subjects	671
EEA total number of subjects	129

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	64
From 65 to 84 years	491
85 years and over	116

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 989 patients were screened, 318 of whom failed screening most commonly due to not meeting inclusion criteria. A total of 671 treatment-naive patients with nAMD were randomized 1:1 into the study: 334 to the faricimab arm and 337 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	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	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).

Arm title	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).

Number of subjects in period 1	Arm A: Faricimab	Arm B: Aflibercept
Started	334	337
Received at Least One Dose of Study Drug	333	336
Completed up to Week 48	319	323
Completed	274	291
Not completed	60	46
Consent withdrawn by subject	25	17
Physician decision	5	2
Adverse event, non-fatal	6	8
Death	13	7
Not Specified	2	4
Lost to follow-up	7	8
Lack of efficacy	2	-

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	334	337	671
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)	34	30	64
From 65-84 years	253	238	491
85 years and over	47	69	116
Age Continuous Units: Years			
arithmetic mean	75.9	76.7	
standard deviation	± 8.6	± 8.8	-
Sex: Female, Male Units: Participants			
Female	191	211	402
Male	143	126	269
Race/Ethnicity, Customized Units: Subjects			
White	303	302	605
Asian	26	28	54
Black or African American	0	3	3
American Indian or Alaska Native	1	2	3

Multiple	1	0	1
Unknown	3	2	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	26	26	52
Not Hispanic or Latino	303	308	611
Unknown or Not Reported	5	3	8
Region of Enrollment Units: Subjects			
United States and Canada	182	184	366
Asia	26	26	52
Rest of the World	126	127	253
Number of Participants by the Eye (Right or Left) Chosen as the Study Eye Units: Subjects			
Right Eye	166	178	344
Left Eye	168	159	327
Number of Participants by the BCVA Letter Score Categories in the Study Eye Units: Subjects			
≥74 Letters	47	52	99
73 to 55 Letters	200	201	401
≤54 Letters	87	84	171
Number of Participants by the Low Luminance Deficit (LLD) Letter Score Categories in the Study Eye Units: Subjects			
<33 Letters	236	235	471
≥33 Letters	95	98	193
Missing/Invalid	3	4	7
Choroidal Neovascularization (CNV) Lesion Type in the Study Eye by Fundus Fluorescein Angiography Units: Subjects			
Occult	177	174	351
Classic	84	73	157
Minimally Classic	32	30	62
Retinal Angiomatous Proliferation (RAP)	14	27	41
Predominantly Classic	17	19	36
Polypoidal Choroidal Vasculopathy (PCV)	6	6	12
Missing	4	8	12
Best Corrected Visual Acuity (BCVA) 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 VisionTM 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	61.3	61.5	
standard deviation	± 12.5	± 12.9	-

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 (≥74, 73-55, and ≤54 letters), baseline LLD (<33 and ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	337		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)	5.8 (4.6 to 7.1)	5.1 (3.9 to 6.4)		

Statistical analyses

Statistical analysis title	Treatment Difference at Weeks 40-48

Statistical analysis description:

The null hypothesis, H0: μ(faricimab) − μ(aflibercept) ≤−4 letters; the alternative hypothesis, Ha: μ(faricimab) − μ(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	671
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Adjusted mean difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.5
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

End point title	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 (≥74, 73-55, and ≤54 letters), baseline LLD (<33 and ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	337		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)	5.4 (4.0 to 6.8)	4.6 (3.3 to 6.0)		

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	671
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted mean difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	0.99

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 (≥74, 73-55, and ≤54 letters), baseline LLD (<33 and ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	337		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 4	4.0 (3.2 to 4.8)	3.6 (2.8 to 4.4)		
Week 8	5.5 (4.6 to 6.4)	4.5 (3.6 to 5.4)		
Week 12	6.4 (5.5 to 7.4)	5.3 (4.4 to 6.2)		
Week 16	6.8 (5.8 to 7.8)	5.2 (4.2 to 6.2)		
Week 20	6.6 (5.5 to 7.6)	4.9 (3.9 to 6.0)		
Week 24	6.4 (5.2 to 7.5)	5.1 (4.0 to 6.3)		
Week 28	6.2 (5.1 to 7.3)	5.6 (4.5 to 6.7)		
Week 32	6.2 (4.9 to 7.4)	5.1 (3.8 to 6.3)		
Week 36	6.5 (5.3 to 7.7)	5.5 (4.3 to 6.7)		
Week 40	6.1 (4.9 to 7.4)	5.1 (3.9 to 6.4)		
Week 44	5.8 (4.5 to 7.1)	5.1 (3.8 to 6.4)		
Week 48	5.5 (4.1 to 6.9)	5.2 (3.8 to 6.5)		
Week 52	5.6 (4.2 to 7.1)	4.5 (3.1 to 5.9)		
Week 56	5.5 (4.1 to 6.9)	4.7 (3.3 to 6.1)		
Week 60	4.9 (3.5 to 6.3)	4.7 (3.2 to 6.1)		
Week 64	5.5 (4.1 to 6.9)	4.8 (3.5 to 6.2)		
Week 68	5.3 (3.9 to 6.8)	4.6 (3.2 to 6.1)		
Week 72	4.8 (3.3 to 6.3)	4.0 (2.5 to 5.4)		
Week 76	4.7 (3.1 to 6.2)	4.4 (2.9 to 5.9)		
Week 80	4.6 (3.1 to 6.1)	3.5 (2.0 to 5.1)		
Week 84	4.5 (3.0 to 6.1)	3.5 (2.0 to 5.1)		
Week 88	4.3 (2.7 to 5.9)	3.7 (2.1 to 5.2)		
Week 92	4.2 (2.6 to 5.9)	3.7 (2.1 to 5.3)		
Week 96	4.2 (2.5 to 5.8)	3.7 (2.0 to 5.3)		
Week 100	4.3 (2.7 to 5.9)	3.6 (2.0 to 5.2)		
Week 104	4.1 (2.5 to 5.8)	3.6 (2.0 to 5.2)		
Week 108	3.6 (1.8 to 5.3)	3.2 (1.5 to 4.9)		
Week 112	3.5 (1.8 to 5.2)	3.1 (1.4 to 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining Greater Than or Equal to (≥)15, ≥10, ≥5, or ≥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 (≥)15, ≥10, ≥5, or ≥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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292[2]	300[3]		
Units: Percentage of participants				
number (confidence interval 95%)				
Gaining ≥15 Letters	20.0 (15.6 to 24.4)	15.7 (11.9 to 19.6)		
Gaining ≥10 Letters	37.1 (31.7 to 42.4)	31.7 (26.7 to 36.8)		
Gaining ≥5 Letters	59.2 (53.7 to 64.7)	58.0 (52.6 to 63.5)		
Gaining ≥0 Letters	75.6 (70.8 to 80.3)	76.8 (72.1 to 81.4)		

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

Statistical analysis title	Gaining ≥15 Letters at Weeks 40-48

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants gaining ≥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	592
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	10.1

Statistical analysis title	Gaining ≥10 Letters at Weeks 40-48

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants gaining ≥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	592
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	12.7

Statistical analysis title	Gaining ≥5 Letters at Weeks 40-48

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants gaining ≥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	592
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	-6.6
upper limit	8.9

Statistical analysis title	Gaining ≥0 Letters at Weeks 40-48

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants gaining ≥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	592
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	-7.9
upper limit	5.4

Secondary: Percentage of Participants Gaining ≥15 Letters from the Baseline BCVA

in the Study Eye Averaged Over Weeks 52, 56, and 60	
End point title	Percentage of Participants Gaining ≥15 Letters from the Baseline BCVA in the Study Eye Averaged Over Weeks 52, 56, and 60

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 52, 56, and 60

End point values	Arm A: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	277[4]	283[5]		
Units: Percentage of participants				
number (confidence interval 95%)	19.2 (15.0 to 23.5)	16.6 (12.5 to 20.6)		

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:

The treatment difference in CMH weighted percentage of participants gaining ≥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	560
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	8.5

Secondary: Percentage of Participants Gaining ≥15 Letters from the Baseline BCVA in the Study Eye Over Time

End point title	Percentage of Participants Gaining ≥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 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[6]	337[7]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	10.1 (6.9 to 13.2)	6.3 (3.8 to 8.8)		
Week 8 (n = 325, 325)	13.7 (10.1 to 17.3)	8.1 (5.3 to 10.9)		
Week 12 (n = 322, 326)	16.7 (12.8 to 20.5)	10.1 (7.0 to 13.1)		
Week 16 (n = 322, 320)	17.7 (13.7 to 21.6)	13.4 (10.0 to 16.9)		
Week 20 (n = 308, 308)	19.1 (14.9 to 23.2)	12.7 (9.1 to 16.2)		
Week 24 (n = 278, 285)	22.1 (17.4 to 26.7)	13.3 (9.6 to 17.0)		
Week 28 (n = 284, 276)	20.8 (16.4 to 25.2)	16.2 (12.1 to 20.3)		
Week 32 (n = 293, 285)	21.6 (17.0 to 26.1)	15.1 (11.3 to 18.9)		
Week 36 (n = 286, 297)	21.4 (16.8 to 26.0)	15.7 (11.8 to 19.6)		
Week 40 (n = 287, 291)	22.1 (17.5 to 26.7)	15.6 (11.7 to 19.5)		
Week 44 (n = 278, 274)	22.2 (17.5 to 26.8)	17.4 (13.2 to 21.6)		
Week 48 (n = 273, 279)	21.2 (16.7 to 25.8)	19.7 (15.3 to 24.0)		
Week 52 (n = 272, 278)	22.5 (17.8 to 27.2)	18.3 (14.0 to 22.7)		
Week 56 (n = 273, 279)	23.1 (18.4 to 27.8)	18.8 (14.6 to 23.0)		
Week 60 (n = 268, 276)	21.3 (16.7 to 25.9)	17.4 (13.3 to 21.5)		
Week 64 (n = 253, 276)	20.3 (15.6 to 25.0)	20.1 (15.7 to 24.6)		
Week 68 (n = 260, 269)	23.2 (18.3 to 28.1)	18.5 (14.1 to 22.8)		

Week 72 (n = 262, 274)	21.1 (16.5 to 25.8)	17.4 (13.1 to 21.6)		
Week 76 (n = 255, 260)	22.9 (18.0 to 27.8)	18.0 (13.7 to 22.3)		
Week 80 (n = 254, 268)	19.7 (14.9 to 24.5)	18.8 (14.4 to 23.2)		
Week 84 (n = 257, 270)	21.1 (16.4 to 25.9)	18.3 (14.0 to 22.5)		
Week 88 (n = 256, 267)	24.6 (19.7 to 29.6)	18.6 (14.3 to 23.0)		
Week 92 (n = 247, 266)	21.4 (16.5 to 26.3)	19.5 (14.9 to 24.0)		
Week 96 (n = 249, 258)	23.0 (18.1 to 27.9)	20.2 (15.7 to 24.6)		
Week 100 (n = 248, 258)	21.5 (16.7 to 26.3)	18.2 (13.9 to 22.5)		
Week 104 (n = 250, 263)	22.9 (17.9 to 27.8)	18.6 (14.2 to 22.9)		
Week 108 (n = 246, 256)	21.9 (17.0 to 26.7)	19.0 (14.6 to 23.4)		
Week 112 (n = 247, 259)	24.0 (19.1 to 29.0)	19.2 (14.6 to 23.7)		

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 ≥10 Letters from the Baseline BCVA in the Study Eye Over Time

End point title	Percentage of Participants Gaining ≥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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[8]	337[9]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	20.1 (16.0 to 24.2)	16.0 (12.3 to 19.7)		
Week 8 (n = 325, 325)	28.6 (23.9 to 33.3)	25.3 (20.9 to 29.8)		
Week 12 (n = 322, 326)	31.4 (26.5 to 36.3)	30.3 (25.5 to 35.1)		
Week 16 (n = 322, 320)	36.9 (31.8 to 41.9)	31.9 (27.0 to 36.7)		
Week 20 (n = 308, 308)	39.1 (34.0 to 44.2)	30.3 (25.4 to 35.2)		
Week 24 (n = 278, 285)	41.4 (36.0 to 46.9)	34.0 (28.7 to 39.3)		
Week 28 (n = 284, 276)	38.9 (33.5 to 44.3)	34.8 (29.5 to 40.1)		
Week 32 (n = 293, 285)	38.6 (33.2 to 44.0)	32.4 (27.2 to 37.7)		
Week 36 (n = 286, 297)	37.1 (31.6 to 42.6)	34.0 (28.8 to 39.2)		
Week 40 (n = 287, 291)	36.9 (31.5 to 42.3)	33.9 (28.6 to 39.2)		
Week 44 (n = 278, 274)	39.5 (33.9 to 45.0)	34.3 (29.0 to 39.7)		
Week 48 (n = 273, 279)	36.8 (31.3 to 42.3)	36.8 (31.4 to 42.2)		
Week 52 (n = 272, 278)	38.7 (33.2 to 44.2)	37.7 (32.2 to 43.2)		
Week 56 (n = 273, 279)	40.3 (34.8 to 45.8)	36.2 (30.8 to 41.6)		
Week 60 (n = 268, 276)	40.1 (34.7 to 45.5)	34.8 (29.4 to 40.3)		
Week 64 (n = 253, 276)	37.2 (31.4 to 43.0)	36.6 (31.1 to 42.0)		
Week 68 (n = 260, 269)	40.0 (34.3 to 45.7)	33.3 (27.8 to 38.7)		
Week 72 (n = 262, 274)	40.1 (34.4 to 45.8)	34.3 (28.8 to 39.8)		
Week 76 (n = 255, 260)	39.4 (33.7 to 45.2)	33.5 (28.0 to 39.0)		
Week 80 (n = 254, 268)	35.5 (29.8 to 41.2)	33.0 (27.7 to 38.4)		
Week 84 (n = 257, 270)	38.2 (32.5 to 43.9)	34.3 (28.9 to 39.7)		
Week 88 (n = 256, 267)	38.9 (33.2 to 44.7)	33.6 (28.3 to 39.0)		
Week 92 (n = 247, 266)	37.8 (31.9 to 43.7)	35.3 (29.7 to 40.8)		
Week 96 (n = 249, 258)	39.6 (33.7 to 45.4)	35.8 (30.3 to 41.4)		
Week 100 (n = 248, 258)	38.5 (32.7 to 44.4)	36.4 (30.8 to 42.0)		
Week 104 (n = 250, 263)	38.7 (32.9 to 44.6)	38.9 (33.3 to 44.5)		
Week 108 (n = 246, 256)	35.1 (29.3 to 40.9)	36.6 (30.9 to 42.2)		

Week 112 (n = 247, 259)	39.5 (33.8 to 45.3)	34.9 (29.3 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[10]	337[11]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	47.6 (42.3 to 52.8)	45.6 (40.4 to 50.9)		
Week 8 (n = 325, 325)	57.8 (52.5 to 63.0)	52.3 (47.2 to 57.5)		
Week 12 (n = 322, 326)	61.5 (56.3 to 66.8)	55.0 (49.7 to 60.2)		
Week 16 (n = 322, 320)	61.8 (56.5 to 67.0)	54.0 (48.7 to 59.3)		
Week 20 (n = 308, 308)	60.2 (54.8 to 65.6)	55.5 (50.0 to 60.9)		
Week 24 (n = 278, 285)	63.4 (57.9 to 68.9)	53.6 (48.0 to 59.3)		
Week 28 (n = 284, 276)	60.8 (55.3 to 66.3)	61.4 (55.8 to 67.0)		
Week 32 (n = 293, 285)	60.5 (55.1 to 65.9)	56.4 (50.8 to 62.0)		
Week 36 (n = 286, 297)	60.5 (55.0 to 66.0)	58.5 (53.0 to 64.0)		

Week 40 (n = 287, 291)	59.1 (53.6 to 64.6)	54.5 (48.9 to 60.2)		
Week 44 (n = 278, 274)	60.3 (54.7 to 65.9)	59.0 (53.3 to 64.6)		
Week 48 (n = 273, 279)	59.3 (53.7 to 65.0)	58.8 (53.2 to 64.4)		
Week 52 (n = 272, 278)	62.6 (57.0 to 68.1)	58.5 (52.8 to 64.1)		
Week 56 (n = 273, 279)	58.6 (53.0 to 64.2)	54.4 (48.7 to 60.2)		
Week 60 (n = 268, 276)	60.4 (54.8 to 66.0)	57.4 (51.6 to 63.1)		
Week 64 (n = 253, 276)	59.3 (53.5 to 65.2)	55.1 (49.3 to 60.9)		
Week 68 (n = 260, 269)	60.4 (54.7 to 66.1)	57.0 (51.2 to 62.7)		
Week 72 (n = 262, 274)	59.8 (54.0 to 65.5)	52.3 (46.5 to 58.1)		
Week 76 (n = 255, 260)	59.3 (53.5 to 65.1)	55.0 (49.1 to 60.9)		
Week 80 (n = 254, 268)	55.2 (49.3 to 61.2)	55.5 (49.6 to 61.3)		
Week 84 (n = 257, 270)	58.4 (52.6 to 64.2)	55.6 (49.8 to 61.4)		
Week 88 (n = 256, 267)	59.3 (53.5 to 65.1)	53.8 (48.0 to 59.6)		
Week 92 (n = 247, 266)	56.8 (50.8 to 62.9)	56.0 (50.3 to 61.8)		
Week 96 (n = 249, 258)	58.2 (52.2 to 64.1)	57.5 (51.7 to 63.4)		
Week 100 (n = 248, 258)	59.1 (53.2 to 65.1)	57.1 (51.2 to 63.0)		
Week 104 (n = 250, 263)	59.8 (54.0 to 65.7)	54.8 (48.9 to 60.7)		
Week 108 (n = 246, 256)	53.6 (47.7 to 59.6)	54.1 (48.2 to 60.1)		
Week 112 (n = 247, 259)	57.3 (51.4 to 63.2)	53.5 (47.6 to 59.5)		

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 ≥0 Letters from the Baseline BCVA in the Study Eye Over Time

End point title	Percentage of Participants Gaining ≥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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[12]	337[13]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	78.9 (74.5 to 83.2)	77.6 (73.3 to 81.9)		
Week 8 (n = 325, 325)	80.7 (76.4 to 84.9)	78.3 (73.9 to 82.7)		
Week 12 (n = 322, 326)	84.2 (80.3 to 88.1)	81.4 (77.3 to 85.6)		
Week 16 (n = 322, 320)	84.8 (80.9 to 88.7)	78.8 (74.6 to 83.1)		
Week 20 (n = 308, 308)	80.8 (76.5 to 85.2)	79.6 (75.2 to 83.9)		
Week 24 (n = 278, 285)	81.9 (77.5 to 86.3)	79.6 (75.1 to 84.1)		
Week 28 (n = 284, 276)	77.8 (73.1 to 82.6)	82.3 (77.9 to 86.7)		
Week 32 (n = 293, 285)	78.7 (74.2 to 83.1)	76.3 (71.5 to 81.0)		
Week 36 (n = 286, 297)	78.9 (74.3 to 83.5)	81.0 (76.6 to 85.4)		
Week 40 (n = 287, 291)	77.1 (72.5 to 81.7)	80.7 (76.3 to 85.2)		
Week 44 (n = 278, 274)	77.0 (72.3 to 81.7)	78.3 (73.6 to 83.0)		
Week 48 (n = 273, 279)	77.0 (72.2 to 81.8)	76.4 (71.5 to 81.3)		
Week 52 (n = 272, 278)	77.4 (72.6 to 82.2)	75.7 (70.7 to 80.6)		
Week 56 (n = 273, 279)	76.3 (71.4 to 81.1)	78.7 (73.9 to 83.5)		
Week 60 (n = 268, 276)	74.4 (69.3 to 79.5)	77.5 (72.6 to 82.3)		
Week 64 (n = 253, 276)	77.7 (72.8 to 82.6)	73.7 (68.6 to 78.8)		
Week 68 (n = 260, 269)	74.9 (69.8 to 80.0)	77.7 (72.8 to 82.6)		
Week 72 (n = 262, 274)	74.9 (69.9 to 79.8)	74.8 (69.8 to 79.8)		
Week 76 (n = 255, 260)	75.7 (70.8 to 80.7)	72.0 (66.6 to 77.4)		
Week 80 (n = 254, 268)	75.5 (70.4 to 80.5)	74.4 (69.3 to 79.5)		
Week 84 (n = 257, 270)	75.5 (70.5 to 80.5)	72.5 (67.3 to 77.7)		
Week 88 (n = 256, 267)	74.8 (69.6 to 80.0)	71.7 (66.4 to 76.9)		
Week 92 (n = 247, 266)	75.0 (69.9 to 80.2)	70.6 (65.3 to 75.9)		

Week 96 (n = 249, 258)	74.7 (69.6 to 79.9)	71.1 (65.7 to 76.5)		
Week 100 (n = 248, 258)	74.6 (69.4 to 79.8)	69.7 (64.2 to 75.2)		
Week 104 (n = 250, 263)	73.8 (68.6 to 79.1)	71.2 (66.0 to 76.5)		
Week 108 (n = 246, 256)	73.4 (68.2 to 78.7)	73.7 (68.4 to 79.0)		
Week 112 (n = 247, 259)	72.8 (67.5 to 78.1)	70.9 (65.5 to 76.3)		

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 ≥15, ≥10, or ≥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 ≥15, ≥10, or ≥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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292[14]	300[15]		
Units: Percentage of participants				
number (confidence interval 95%)				
Avoiding a Loss of ≥15 Letters	95.4 (93.0 to 97.7)	94.1 (91.5 to 96.7)		
Avoiding a Loss of ≥10 Letters	91.6 (88.6 to 94.7)	92.0 (89.1 to 95.0)		
Avoiding a Loss of ≥5 Letters	88.0 (84.3 to 91.6)	86.8 (83.0 to 90.5)		

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

Statistical analysis title	Avoiding a Loss of ≥15 Letters at Weeks 40-48
Statistical analysis description:	
The treatment difference in CMH weighted percentage of participants avoiding a loss of ≥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	592
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	4.8

Statistical analysis title	Avoiding a Loss of ≥5 Letters at Weeks 40-48
Statistical analysis description:	
The treatment difference in CMH weighted percentage of participants avoiding a loss of ≥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	592
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	-4
upper limit	6.4

Statistical analysis title	Avoiding a Loss of ≥10 Letters at Weeks 40-48
Statistical analysis description:	
The treatment difference in CMH weighted percentage of participants avoiding a loss of ≥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	592
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	-4.6
upper limit	3.9

Secondary: Percentage of Participants Avoiding a Loss of ≥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 ≥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 (≥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 52, 56, and 60

End point values	Arm A: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	277[16]	283[17]		
Units: Percentage of participants				
number (confidence interval 95%)	93.9 (91.3 to 96.5)	94.1 (91.4 to 96.8)		

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 ≥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	560
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	3.6

Secondary: Percentage of Participants Avoiding a Loss of ≥15 Letters from the Baseline BCVA in the Study Eye Over Time

End point title	Percentage of Participants Avoiding a Loss of ≥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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[18]	337[19]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	97.6 (95.9 to 99.2)	99.0 (98.0 to 100.0)		
Week 8 (n = 325, 325)	97.6 (96.0 to 99.2)	98.7 (97.6 to 99.9)		
Week 12 (n = 322, 326)	98.2 (96.7 to 99.6)	97.5 (95.8 to 99.1)		
Week 16 (n = 322, 320)	98.1 (96.7 to 99.6)	97.0 (95.3 to 98.8)		
Week 20 (n = 308, 308)	97.4 (95.7 to 99.1)	94.9 (92.5 to 97.3)		
Week 24 (n = 278, 285)	97.2 (95.3 to 99.1)	97.5 (95.8 to 99.3)		
Week 28 (n = 284, 276)	95.9 (93.8 to 98.1)	96.7 (94.6 to 98.8)		
Week 32 (n = 293, 285)	95.4 (93.1 to 97.7)	95.7 (93.5 to 98.0)		
Week 36 (n = 286, 297)	95.2 (92.8 to 97.6)	95.4 (93.1 to 97.7)		
Week 40 (n = 287, 291)	96.6 (94.5 to 98.6)	94.2 (91.6 to 96.8)		
Week 44 (n = 278, 274)	95.7 (93.5 to 98.0)	93.9 (91.2 to 96.6)		
Week 48 (n = 273, 279)	94.0 (91.3 to 96.7)	93.3 (90.4 to 96.1)		
Week 52 (n = 272, 278)	93.5 (90.8 to 96.2)	93.5 (90.7 to 96.3)		
Week 56 (n = 273, 279)	94.7 (92.2 to 97.2)	95.0 (92.5 to 97.5)		

Week 60 (n = 268, 276)	93.6 (90.8 to 96.4)	92.6 (89.7 to 95.6)		
Week 64 (n = 253, 276)	94.1 (91.3 to 96.9)	92.9 (89.9 to 95.9)		
Week 68 (n = 260, 269)	92.6 (89.6 to 95.6)	92.9 (89.9 to 95.8)		
Week 72 (n = 262, 274)	93.5 (90.7 to 96.3)	91.3 (88.2 to 94.4)		
Week 76 (n = 255, 260)	94.2 (91.6 to 96.8)	92.7 (89.8 to 95.7)		
Week 80 (n = 254, 268)	93.6 (90.9 to 96.4)	90.7 (87.4 to 93.9)		
Week 84 (n = 257, 270)	92.8 (89.9 to 95.7)	91.5 (88.4 to 94.5)		
Week 88 (n = 256, 267)	93.1 (90.3 to 96.0)	90.4 (87.2 to 93.7)		
Week 92 (n = 247, 266)	92.1 (89.1 to 95.2)	93.2 (90.5 to 95.9)		
Week 96 (n = 249, 258)	91.6 (88.4 to 94.8)	88.9 (85.3 to 92.5)		
Week 100 (n = 248, 258)	92.7 (89.8 to 95.6)	89.5 (86.0 to 93.0)		
Week 104 (n = 250, 263)	93.2 (90.3 to 96.1)	90.7 (87.4 to 93.9)		
Week 108 (n = 246, 256)	92.0 (88.9 to 95.1)	89.6 (86.0 to 93.2)		
Week 112 (n = 247, 259)	90.6 (87.3 to 93.9)	88.8 (85.1 to 92.4)		

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 ≥10 Letters from the Baseline BCVA in the Study Eye Over Time

End point title	Percentage of Participants Avoiding a Loss of ≥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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[20]	337[21]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	95.1 (92.9 to 97.4)	96.2 (94.3 to 98.2)		
Week 8 (n = 325, 325)	96.0 (94.0 to 98.0)	96.9 (95.1 to 98.7)		
Week 12 (n = 322, 326)	96.3 (94.4 to 98.3)	95.5 (93.3 to 97.7)		
Week 16 (n = 322, 320)	95.1 (92.8 to 97.4)	92.6 (89.9 to 95.4)		
Week 20 (n = 308, 308)	93.9 (91.3 to 96.5)	92.7 (89.9 to 95.4)		
Week 24 (n = 278, 285)	94.3 (91.7 to 96.9)	94.4 (91.9 to 96.9)		
Week 28 (n = 284, 276)	93.5 (90.8 to 96.2)	94.9 (92.3 to 97.4)		
Week 32 (n = 293, 285)	92.5 (89.6 to 95.3)	92.9 (89.9 to 95.8)		
Week 36 (n = 286, 297)	93.2 (90.3 to 96.0)	91.7 (88.6 to 94.7)		
Week 40 (n = 287, 291)	92.2 (89.2 to 95.2)	91.8 (88.8 to 94.8)		
Week 44 (n = 278, 274)	92.3 (89.4 to 95.3)	90.9 (87.7 to 94.2)		
Week 48 (n = 273, 279)	91.5 (88.3 to 94.6)	91.5 (88.3 to 94.7)		
Week 52 (n = 272, 278)	91.7 (88.6 to 94.7)	91.1 (87.8 to 94.4)		
Week 56 (n = 273, 279)	92.3 (89.3 to 95.3)	90.4 (87.0 to 93.8)		
Week 60 (n = 268, 276)	90.7 (87.5 to 94.0)	88.5 (85.0 to 92.1)		
Week 64 (n = 253, 276)	91.3 (88.0 to 94.6)	90.3 (87.0 to 93.7)		
Week 68 (n = 260, 269)	92.2 (89.2 to 95.3)	90.3 (86.9 to 93.7)		
Week 72 (n = 262, 274)	89.6 (86.2 to 93.1)	88.1 (84.6 to 91.7)		
Week 76 (n = 255, 260)	89.2 (85.6 to 92.7)	88.0 (84.3 to 91.8)		
Week 80 (n = 254, 268)	89.3 (85.7 to 92.9)	86.4 (82.6 to 90.2)		
Week 84 (n = 257, 270)	89.0 (85.5 to 92.5)	86.9 (83.2 to 90.7)		
Week 88 (n = 256, 267)	89.2 (85.7 to 92.7)	85.2 (81.2 to 89.3)		
Week 92 (n = 247, 266)	87.7 (83.8 to 91.6)	86.3 (82.4 to 90.1)		
Week 96 (n = 249, 258)	87.8 (84.0 to 91.5)	85.7 (81.6 to 89.8)		
Week 100 (n = 248, 258)	88.6 (84.9 to 92.3)	86.1 (82.1 to 90.1)		
Week 104 (n = 250, 263)	87.6 (83.7 to 91.5)	85.3 (81.3 to 89.4)		
Week 108 (n = 246, 256)	85.2 (81.1 to 89.4)	87.3 (83.4 to 91.2)		

Week 112 (n = 247, 259)	84.7 (80.5 to 88.9)	84.2 (79.9 to 88.5)		

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 ≥5 Letters from the Baseline BCVA in the Study Eye Over Time

End point title	Percentage of Participants Avoiding a Loss of ≥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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[22]	337[23]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	90.5 (87.4 to 93.6)	90.6 (87.5 to 93.6)		
Week 8 (n = 325, 325)	92.3 (89.6 to 95.1)	90.6 (87.5 to 93.7)		
Week 12 (n = 322, 326)	92.2 (89.4 to 95.1)	88.8 (85.4 to 92.1)		
Week 16 (n = 322, 320)	90.4 (87.3 to 93.6)	87.4 (83.8 to 90.9)		
Week 20 (n = 308, 308)	89.3 (85.9 to 92.7)	87.1 (83.5 to 90.7)		
Week 24 (n = 278, 285)	89.1 (85.6 to 92.6)	88.8 (85.3 to 92.3)		
Week 28 (n = 284, 276)	88.2 (84.6 to 91.9)	90.2 (86.7 to 93.6)		
Week 32 (n = 293, 285)	87.0 (83.3 to 90.7)	85.8 (81.9 to 89.6)		
Week 36 (n = 286, 297)	88.3 (84.7 to 91.9)	86.7 (82.9 to 90.4)		
Week 40 (n = 287, 291)	86.8 (83.1 to 90.6)	87.4 (83.7 to 91.1)		

Week 44 (n = 278, 274)	85.2 (81.3 to 89.2)	85.3 (81.2 to 89.4)		
Week 48 (n = 273, 279)	85.6 (81.6 to 89.6)	83.5 (79.3 to 87.7)		
Week 52 (n = 272, 278)	84.8 (80.7 to 88.9)	85.5 (81.4 to 89.6)		
Week 56 (n = 273, 279)	84.4 (80.4 to 88.5)	83.7 (79.4 to 88.0)		
Week 60 (n = 268, 276)	81.5 (77.0 to 85.9)	84.5 (80.4 to 88.6)		
Week 64 (n = 253, 276)	87.8 (84.0 to 91.7)	85.3 (81.3 to 89.4)		
Week 68 (n = 260, 269)	85.0 (80.9 to 89.1)	87.0 (83.1 to 90.9)		
Week 72 (n = 262, 274)	84.2 (80.0 to 88.3)	81.1 (76.6 to 85.6)		
Week 76 (n = 255, 260)	83.5 (79.1 to 87.8)	83.3 (78.9 to 87.7)		
Week 80 (n = 254, 268)	81.0 (76.3 to 85.6)	81.9 (77.5 to 86.4)		
Week 84 (n = 257, 270)	82.6 (78.2 to 86.9)	81.8 (77.4 to 86.3)		
Week 88 (n = 256, 267)	80.8 (76.2 to 85.4)	78.8 (74.1 to 83.6)		
Week 92 (n = 247, 266)	81.7 (77.1 to 86.3)	79.2 (74.5 to 83.9)		
Week 96 (n = 249, 258)	82.1 (77.6 to 86.6)	78.1 (73.2 to 83.0)		
Week 100 (n = 248, 258)	81.7 (77.1 to 86.3)	80.1 (75.4 to 84.8)		
Week 104 (n = 250, 263)	79.6 (74.7 to 84.4)	80.5 (75.8 to 85.1)		
Week 108 (n = 246, 256)	79.7 (74.9 to 84.4)	80.7 (75.9 to 85.4)		
Week 112 (n = 247, 259)	78.6 (73.7 to 83.4)	78.9 (74.1 to 83.7)		

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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292[24]	300[25]		
Units: Percentage of participants				
number (confidence interval 95%)	24.3 (19.5 to 29.1)	21.3 (16.8 to 25.7)		

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 ≥15 letters or achieving BCVA ≥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	592
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	9.5

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 Over Time

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 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[26]	337[27]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	11.0 (7.7 to 14.3)	8.1 (5.3 to 10.9)		
Week 8 (n = 325, 325)	16.3 (12.3 to 20.2)	11.1 (7.8 to 14.4)		
Week 12 (n = 322, 326)	20.4 (16.2 to 24.7)	14.9 (11.2 to 18.6)		
Week 16 (n = 322, 320)	20.5 (16.3 to 24.8)	17.3 (13.4 to 21.3)		
Week 20 (n = 308, 308)	22.4 (17.9 to 26.9)	17.7 (13.5 to 21.8)		
Week 24 (n = 278, 285)	25.5 (20.5 to 30.5)	19.1 (14.7 to 23.4)		
Week 28 (n = 284, 276)	25.7 (20.8 to 30.5)	20.0 (15.5 to 24.5)		
Week 32 (n = 293, 285)	27.3 (22.4 to 32.3)	21.9 (17.3 to 26.5)		
Week 36 (n = 286, 297)	27.2 (22.1 to 32.2)	23.7 (19.0 to 28.4)		
Week 40 (n = 287, 291)	26.0 (21.0 to 30.9)	21.4 (16.8 to 25.9)		
Week 44 (n = 278, 274)	26.5 (21.5 to 31.6)	22.8 (18.1 to 27.5)		
Week 48 (n = 273, 279)	24.9 (20.0 to 29.8)	27.6 (22.5 to 32.6)		
Week 52 (n = 272, 278)	25.0 (20.1 to 30.0)	23.8 (19.0 to 28.7)		
Week 56 (n = 273, 279)	26.4 (21.4 to 31.5)	24.4 (19.7 to 29.1)		
Week 60 (n = 268, 276)	25.2 (20.2 to 30.2)	22.7 (18.1 to 27.4)		
Week 64 (n = 253, 276)	24.2 (19.1 to 29.3)	25.6 (20.6 to 30.5)		
Week 68 (n = 260, 269)	27.5 (22.2 to 32.8)	24.3 (19.4 to 29.2)		
Week 72 (n = 262, 274)	26.1 (21.0 to 31.2)	24.2 (19.4 to 29.0)		
Week 76 (n = 255, 260)	27.6 (22.2 to 32.9)	23.6 (18.8 to 28.5)		
Week 80 (n = 254, 268)	24.1 (18.9 to 29.3)	25.9 (20.9 to 31.0)		
Week 84 (n = 257, 270)	26.2 (21.0 to 31.4)	23.8 (19.0 to 28.7)		
Week 88 (n = 256, 267)	29.4 (24.0 to 34.7)	25.0 (19.9 to 30.0)		
Week 92 (n = 247, 266)	27.7 (22.2 to 33.1)	27.3 (22.1 to 32.6)		

Week 96 (n = 249, 258)	28.0 (22.6 to 33.3)	26.7 (21.7 to 31.8)		
Week 100 (n = 248, 258)	27.3 (22.0 to 32.7)	24.4 (19.5 to 29.3)		
Week 104 (n = 250, 263)	27.9 (22.5 to 33.3)	23.9 (18.9 to 28.8)		
Week 108 (n = 246, 256)	27.3 (21.9 to 32.6)	24.2 (19.3 to 29.1)		
Week 112 (n = 247, 259)	26.9 (21.6 to 32.1)	25.5 (20.4 to 30.6)		

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 ≥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 ≥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. ≥69 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

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 40, 44, and 48

End point values	Arm A: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292[28]	300[29]		
Units: Percentage of participants				
number (confidence interval 95%)	56.4 (51.5 to 61.4)	57.0 (51.9 to 62.1)		

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 ≥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	592
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	6.6

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

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA ≥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. ≥69 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[30]	337[31]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	52.8 (48.4 to 57.2)	50.5 (46.4 to 54.7)		
Week 8 (n = 325, 325)	54.5 (49.9 to 59.1)	50.7 (46.3 to 55.1)		
Week 12 (n = 322, 326)	58.3 (53.7 to 62.9)	53.4 (48.8 to 58.0)		
Week 16 (n = 322, 320)	60.4 (55.6 to 65.2)	53.7 (49.1 to 58.3)		
Week 20 (n = 308, 308)	59.5 (54.6 to 64.5)	54.4 (49.6 to 59.1)		
Week 24 (n = 278, 285)	59.4 (54.3 to 64.5)	54.4 (49.4 to 59.4)		

Week 28 (n = 284, 276)	57.5 (52.4 to 62.6)	59.0 (53.8 to 64.1)		
Week 32 (n = 293, 285)	57.7 (52.7 to 62.8)	58.0 (52.8 to 63.1)		
Week 36 (n = 286, 297)	59.7 (54.8 to 64.7)	59.6 (54.5 to 64.7)		
Week 40 (n = 287, 291)	57.5 (52.4 to 62.7)	58.0 (52.8 to 63.1)		
Week 44 (n = 278, 274)	59.9 (54.8 to 65.0)	59.4 (54.1 to 64.7)		
Week 48 (n = 273, 279)	58.9 (53.7 to 64.1)	58.1 (52.7 to 63.6)		
Week 52 (n = 272, 278)	61.0 (55.8 to 66.1)	57.4 (52.0 to 62.9)		
Week 56 (n = 273, 279)	59.0 (53.8 to 64.2)	55.9 (50.5 to 61.3)		
Week 60 (n = 268, 276)	57.9 (52.4 to 63.4)	56.8 (51.4 to 62.2)		
Week 64 (n = 253, 276)	62.5 (57.1 to 67.9)	57.7 (52.3 to 63.0)		
Week 68 (n = 260, 269)	61.0 (55.6 to 66.4)	59.3 (54.0 to 64.6)		
Week 72 (n = 262, 274)	59.5 (54.0 to 65.0)	57.3 (52.0 to 62.6)		
Week 76 (n = 255, 260)	58.4 (52.9 to 63.9)	55.3 (49.9 to 60.6)		
Week 80 (n = 254, 268)	56.8 (51.2 to 62.4)	55.5 (50.1 to 60.9)		
Week 84 (n = 257, 270)	57.6 (52.1 to 63.1)	58.0 (52.6 to 63.3)		
Week 88 (n = 256, 267)	59.1 (53.5 to 64.8)	54.1 (48.5 to 59.7)		
Week 92 (n = 247, 266)	58.6 (52.9 to 64.2)	57.8 (52.3 to 63.2)		
Week 96 (n = 249, 258)	59.3 (53.7 to 64.9)	58.3 (52.6 to 64.0)		
Week 100 (n = 248, 258)	58.1 (52.5 to 63.8)	57.4 (51.9 to 63.0)		
Week 104 (n = 250, 263)	59.8 (54.2 to 65.5)	58.0 (52.4 to 63.6)		
Week 108 (n = 246, 256)	56.4 (50.7 to 62.1)	56.4 (50.9 to 62.0)		
Week 112 (n = 247, 259)	56.3 (50.4 to 62.2)	54.3 (48.6 to 59.9)		

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 ≤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 ≤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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292[32]	300[33]		
Units: Percentage of participants				
number (confidence interval 95%)	6.4 (3.7 to 9.1)	6.9 (4.2 to 9.5)		

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

Statistical analysis title	Treatment Difference at Weeks 40-48

Statistical analysis description:

The treatment difference in CMH weighted percentage of participants with BCVA ≤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	592
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	3.3

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

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA ≤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 (≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[34]	337[35]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 327, 331)	5.5 (3.2 to 7.9)	5.5 (3.2 to 7.7)		
Week 8 (n = 325, 325)	5.8 (3.4 to 8.3)	5.9 (3.6 to 8.2)		
Week 12 (n = 322, 326)	4.6 (2.5 to 6.8)	5.6 (3.3 to 7.9)		
Week 16 (n = 322, 320)	5.8 (3.5 to 8.2)	6.3 (3.9 to 8.8)		
Week 20 (n = 308, 308)	5.9 (3.5 to 8.4)	6.9 (4.3 to 9.5)		
Week 24 (n = 278, 285)	4.3 (2.0 to 6.6)	5.9 (3.4 to 8.5)		
Week 28 (n = 284, 276)	5.4 (3.0 to 7.9)	5.2 (2.8 to 7.7)		
Week 32 (n = 293, 285)	6.1 (3.5 to 8.7)	6.8 (4.2 to 9.4)		
Week 36 (n = 286, 297)	6.4 (3.7 to 9.1)	6.7 (4.1 to 9.3)		
Week 40 (n = 287, 291)	7.1 (4.3 to 9.9)	8.1 (5.3 to 11.0)		
Week 44 (n = 278, 274)	7.0 (4.1 to 9.9)	6.7 (4.0 to 9.3)		
Week 48 (n = 273, 279)	7.4 (4.4 to 10.4)	7.8 (4.9 to 10.7)		
Week 52 (n = 272, 278)	8.1 (5.0 to 11.1)	9.4 (6.3 to 12.6)		
Week 56 (n = 273, 279)	6.3 (3.6 to 9.0)	7.6 (4.7 to 10.5)		
Week 60 (n = 268, 276)	6.9 (4.0 to 9.8)	8.7 (5.6 to 11.7)		
Week 64 (n = 253, 276)	7.8 (4.6 to 11.0)	9.1 (6.0 to 12.3)		
Week 68 (n = 260, 269)	7.6 (4.5 to 10.7)	9.3 (6.2 to 12.5)		
Week 72 (n = 262, 274)	8.6 (5.4 to 11.8)	10.7 (7.5 to 13.9)		
Week 76 (n = 255, 260)	7.9 (4.7 to 11.1)	10.8 (7.5 to 14.2)		
Week 80 (n = 254, 268)	8.8 (5.5 to 12.0)	10.6 (7.2 to 13.9)		
Week 84 (n = 257, 270)	7.7 (4.6 to 10.8)	11.0 (7.8 to 14.2)		
Week 88 (n = 256, 267)	9.5 (6.1 to 12.9)	11.7 (8.3 to 15.0)		
Week 92 (n = 247, 266)	9.0 (5.6 to 12.5)	12.4 (9.0 to 15.7)		
Week 96 (n = 249, 258)	8.6 (5.3 to 12.0)	11.7 (8.2 to 15.1)		
Week 100 (n = 248, 258)	8.3 (5.0 to 11.5)	11.9 (8.4 to 15.4)		

Week 104 (n = 250, 263)	9.4 (6.0 to 12.9)	11.7 (8.3 to 15.1)		
Week 108 (n = 246, 256)	7.7 (4.5 to 10.9)	10.4 (7.1 to 13.7)		
Week 112 (n = 247, 259)	8.2 (4.9 to 11.5)	11.8 (8.3 to 15.2)		

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[36]

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: Faricimab			
Subject group type	Reporting group			
Number of subjects analysed	315			
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 8 Weeks	20.3 (15.9 to 24.8)			
Once Every 12 Weeks	34.0 (28.7 to 39.2)			
Once Every 16 Weeks	45.7 (40.2 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 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[37]

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: Faricimab			
Subject group type	Reporting group			
Number of subjects analysed	302			
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 8 Weeks	20.2 (15.7 to 24.7)			
Once Every 12 Weeks	33.4 (28.1 to 38.8)			
Once Every 16 Weeks	46.4 (40.7 to 52.0)			

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[38]

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: Faricimab			
Subject group type	Reporting group			
Number of subjects analysed	271			
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 8 Weeks	25.8 (20.6 to 31.0)			
Once Every 12 Weeks	15.1 (10.9 to 19.4)			
Once Every 16 Weeks	59.0 (53.2 to 64.9)			

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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	336		
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 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	336		
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 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	336		
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 Study Eye Averaged Over Weeks 40, 44, and 48

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 (≥74 letters, 73-55 letters, and ≤54 letters), baseline LLD (<33 letters and ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	337		
Units: microns				
arithmetic mean (confidence interval 95%)	-136.8 (-142.6 to -131.0)	-129.4 (-135.2 to -123.5)		

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	671
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted mean difference
Point estimate	-7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.7
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	4.19

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 Study Eye Averaged Over Weeks 52, 56, and 60

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 (≥74 letters, 73-55 letters, and ≤54 letters), baseline LLD (<33 letters and ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	337		
Units: microns				
arithmetic mean (confidence interval 95%)	-134.5 (-140.5 to -128.6)	-135.5 (-141.5 to -129.6)		

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	671
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted mean difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.4
upper limit	9.4
Variability estimate	Standard error of the mean
Dispersion value	4.26

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 Study Eye Over Time

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 (≥74 letters, 73-55 letters, and ≤54 letters), baseline LLD (<33 letters and ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	337		
Units: microns				
arithmetic mean (confidence interval 95%)				
Week 4	-131.7 (-137.9 to -125.4)	-116.3 (-122.5 to -110.1)		
Week 8	-142.6 (-148.1 to -137.2)	-131.8 (-137.2 to -126.3)		
Week 12	-149.0 (-154.1 to -143.9)	-136.1 (-141.2 to -131.1)		
Week 16	-148.7 (-155.1 to -142.3)	-110.4 (-116.8 to -104.0)		
Week 20	-132.9 (-139.2 to -126.6)	-136.1 (-142.4 to -129.8)		
Week 24	-128.8 (-135.9 to -121.8)	-115.5 (-122.6 to -108.5)		
Week 28	-129.1 (-135.5 to -122.8)	-132.5 (-139.0 to -126.1)		
Week 32	-142.7 (-150.2 to -135.2)	-114.5 (-122.0 to -107.0)		
Week 36	-132.8 (-138.9 to -126.7)	-139.1 (-145.2 to -133.1)		
Week 40	-140.8 (-148.0 to -133.7)	-123.9 (-131.0 to -116.7)		
Week 44	-133.9 (-139.9 to -128.0)	-142.4 (-148.3 to -136.4)		
Week 48	-138.1 (-145.1 to -131.2)	-126.0 (-132.9 to -119.1)		
Week 52	-139.9 (-146.2 to -133.6)	-139.6 (-145.9 to -133.3)		
Week 56	-140.4 (-147.4 to -133.3)	-125.9 (-133.0 to -118.9)		
Week 60	-124.1 (-131.1 to -117.1)	-143.5 (-150.4 to -136.5)		
Week 64	-145.4 (-152.4 to -138.4)	-127.8 (-134.7 to -120.9)		
Week 68	-137.5 (-144.0 to -130.9)	-142.8 (-149.4 to -136.3)		
Week 72	-139.7 (-147.2 to -132.3)	-132.0 (-139.4 to -124.7)		
Week 76	-135.3 (-142.2 to -128.3)	-142.8 (-149.8 to -135.9)		

Week 80	-146.7 (-154.3 to -139.0)	-132.1 (-139.7 to -124.5)		
Week 84	-141.7 (-148.4 to -135.0)	-143.2 (-149.9 to -136.6)		
Week 88	-143.9 (-150.7 to -137.2)	-139.3 (-146.0 to -132.6)		
Week 92	-144.8 (-151.1 to -138.4)	-148.5 (-154.7 to -142.2)		
Week 96	-147.6 (-154.6 to -140.5)	-139.7 (-146.7 to -132.8)		
Week 100	-145.7 (-152.7 to -138.7)	-147.1 (-153.9 to -140.2)		
Week 104	-147.7 (-154.6 to -140.8)	-143.4 (-150.2 to -136.6)		
Week 108	-141.7 (-148.5 to -134.8)	-151.0 (-157.7 to -144.2)		
Week 112	-150.1 (-157.1 to -143.1)	-144.3 (-151.3 to -137.4)		

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 (≥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 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[39]	337[40]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 324, 332)	89.2 (86.0 to 92.4)	85.2 (81.6 to 88.8)		
Week 8 (n = 321, 325)	87.5 (84.1 to 90.9)	84.3 (80.6 to 88.1)		
Week 12 (n = 320, 323)	89.3 (86.1 to 92.5)	85.4 (81.8 to 89.0)		

Week 16 (n = 318, 315)	89.2 (86.0 to 92.5)	76.3 (71.8 to 80.8)		
Week 20 (n = 307, 306)	82.4 (78.3 to 86.5)	83.4 (79.5 to 87.3)		
Week 24 (n = 279, 284)	80.5 (75.9 to 85.0)	77.7 (73.0 to 82.4)		
Week 28 (n = 285, 276)	76.9 (72.3 to 81.4)	85.3 (81.3 to 89.2)		
Week 32 (n = 291, 285)	86.8 (83.1 to 90.6)	79.1 (74.6 to 83.7)		
Week 36 (n = 284, 295)	79.9 (75.5 to 84.3)	83.5 (79.4 to 87.6)		
Week 40 (n = 276, 285)	82.1 (77.7 to 86.5)	77.2 (72.5 to 81.9)		
Week 44 (n = 273, 264)	75.5 (70.6 to 80.3)	84.9 (80.7 to 89.1)		
Week 48 (n = 263, 267)	82.1 (77.7 to 86.5)	74.4 (69.4 to 79.5)		
Week 52 (n = 273, 277)	83.1 (78.8 to 87.4)	85.0 (80.9 to 89.1)		
Week 56 (n = 271, 276)	84.9 (80.8 to 89.1)	80.3 (75.8 to 84.9)		
Week 60 (n = 265, 264)	72.9 (67.9 to 77.9)	82.3 (77.9 to 86.7)		
Week 104 (n = 249, 263)	80.0 (75.2 to 84.8)	80.7 (76.1 to 85.4)		
Week 108 (n = 243, 253)	77.8 (72.9 to 82.7)	84.7 (80.5 to 88.9)		
Week 112 (n = 245, 256)	82.3 (77.7 to 86.9)	76.2 (71.0 to 81.3)		

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 (≥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 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[41]	337[42]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 324, 332)	67.8 (62.9 to 72.7)	58.8 (53.7 to 64.0)		
Week 8 (n = 321, 324)	84.5 (80.6 to 88.4)	76.4 (71.9 to 81.0)		
Week 12 (n = 321, 324)	87.2 (83.6 to 90.8)	78.5 (74.1 to 82.9)		
Week 16 (n = 318, 316)	89.6 (86.3 to 92.9)	59.9 (54.6 to 65.2)		
Week 20 (n = 307, 307)	75.1 (70.3 to 79.9)	76.3 (71.6 to 81.0)		
Week 24 (n = 279, 284)	70.8 (65.6 to 75.9)	63.9 (58.4 to 69.4)		
Week 28 (n = 285, 276)	71.1 (65.9 to 76.2)	78.8 (74.0 to 83.5)		
Week 32 (n = 292, 285)	82.2 (77.9 to 86.5)	65.1 (59.6 to 70.6)		
Week 36 (n = 285, 295)	74.1 (69.2 to 79.1)	79.9 (75.4 to 84.4)		
Week 40 (n = 284, 288)	78.5 (73.9 to 83.1)	67.3 (61.9 to 72.7)		
Week 44 (n = 277, 274)	69.6 (64.3 to 74.9)	78.0 (73.1 to 82.8)		
Week 48 (n = 268, 279)	75.7 (70.7 to 80.8)	65.8 (60.4 to 71.1)		
Week 52 (n = 273, 278)	80.6 (76.0 to 85.2)	79.9 (75.3 to 84.5)		
Week 56 (n = 271, 276)	79.0 (74.3 to 83.7)	70.1 (64.7 to 75.4)		
Week 60 (n = 267, 274)	67.7 (62.2 to 73.2)	77.5 (72.6 to 82.3)		
Week 104 (n = 249, 261)	79.3 (74.5 to 84.2)	74.9 (69.7 to 80.1)		
Week 108 (n = 245, 253)	79.6 (74.6 to 84.6)	77.4 (72.4 to 82.5)		
Week 112 (n = 245, 256)	80.9 (76.1 to 85.7)	73.1 (67.7 to 78.4)		

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 millimetre [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 (≥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

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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[43]	337[44]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 323, 332)	60.8 (55.7 to 66.0)	49.0 (43.8 to 54.2)		
Week 8 (n = 321, 324)	74.5 (69.9 to 79.2)	63.1 (58.0 to 68.2)		
Week 12 (n = 319, 323)	77.4 (72.9 to 81.9)	66.3 (61.4 to 71.3)		
Week 16 (n = 318, 315)	78.8 (74.4 to 83.2)	44.0 (38.6 to 49.4)		
Week 20 (n = 307, 306)	64.7 (59.4 to 70.0)	62.2 (56.9 to 67.4)		
Week 24 (n = 279, 284)	57.2 (51.6 to 62.9)	48.9 (43.2 to 54.6)		
Week 28 (n = 285, 276)	54.8 (49.2 to 60.5)	66.9 (61.5 to 72.3)		
Week 32 (n = 292, 285)	71.9 (66.8 to 77.0)	51.2 (45.5 to 56.9)		
Week 36 (n = 285, 295)	59.4 (53.7 to 65.1)	66.6 (61.3 to 71.9)		
Week 40 (n = 278, 286)	64.8 (59.3 to 70.3)	52.1 (46.3 to 57.9)		
Week 44 (n = 275, 266)	51.4 (45.6 to 57.2)	65.5 (59.8 to 71.1)		
Week 48 (n = 264, 268)	63.3 (57.6 to 68.9)	47.1 (41.3 to 52.9)		
Week 52 (n = 273, 277)	68.4 (63.0 to 73.8)	68.4 (63.1 to 73.8)		
Week 56 (n = 271, 276)	67.8 (62.3 to 73.3)	55.3 (49.4 to 61.1)		
Week 60 (n = 266, 267)	48.6 (42.7 to 54.4)	62.4 (56.7 to 68.2)		
Week 104 (n = 249, 261)	63.0 (57.0 to 68.9)	59.0 (53.1 to 65.0)		
Week 108 (n = 243, 253)	60.7 (54.7 to 66.8)	63.6 (57.8 to 69.4)		
Week 112 (n = 244, 256)	65.9 (60.0 to 71.8)	54.5 (48.4 to 60.6)		

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 (≥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 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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334[45]	337[46]		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 325, 332)	5.3 (2.9 to 7.6)	4.9 (2.6 to 7.2)		
Week 8 (n = 320, 325)	3.5 (1.5 to 5.5)	4.3 (2.1 to 6.5)		
Week 12 (n = 322, 325)	2.9 (1.0 to 4.7)	2.1 (0.6 to 3.7)		
Week 16 (n = 318, 316)	1.6 (0.2 to 3.0)	4.4 (2.2 to 6.6)		
Week 20 (n = 306, 309)	2.4 (0.7 to 4.1)	3.9 (1.8 to 6.1)		
Week 24 (n = 279, 285)	3.3 (1.2 to 5.4)	4.2 (1.9 to 6.6)		
Week 28 (n = 285, 276)	2.9 (1.0 to 4.8)	5.8 (3.1 to 8.5)		
Week 32 (n = 292, 285)	3.4 (1.4 to 5.5)	3.6 (1.4 to 5.7)		
Week 36 (n = 285, 295)	4.3 (1.9 to 6.6)	6.4 (3.7 to 9.2)		
Week 40 (n = 284, 291)	7.8 (4.7 to 10.9)	9.9 (6.5 to 13.3)		
Week 44 (n = 277, 273)	3.6 (1.5 to 5.8)	8.8 (5.5 to 12.2)		
Week 48 (n = 270, 279)	3.4 (1.3 to 5.5)	7.7 (4.6 to 10.7)		
Week 52 (n = 273, 278)	2.3 (0.5 to 4.1)	3.5 (1.4 to 5.7)		
Week 56 (n = 271, 276)	2.6 (0.7 to 4.5)	5.8 (3.0 to 8.5)		
Week 60 (n = 267, 274)	4.2 (1.8 to 6.5)	6.4 (3.6 to 9.2)		
Week 104 (n = 249, 263)	3.7 (1.4 to 6.0)	4.9 (2.3 to 7.6)		
Week 108 (n = 243, 252)	3.1 (0.9 to 5.4)	7.5 (4.2 to 10.7)		
Week 112 (n = 246, 256)	4.0 (1.6 to 6.4)	8.0 (4.7 to 11.2)		

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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[47]	0[48]		
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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	248		
Units: millimetres squared (mm^2)				
arithmetic mean (standard deviation)	0.0 (± 4.5)	0.4 (± 4.8)		

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:

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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	246		
Units: millimetres squared (mm^2)				
arithmetic mean (standard deviation)	-3.8 (± 6.9)	-3.0 (± 6.9)		

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:

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 112

End point values	Arm A: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	236		
Units: millimetres squared (mm^2)				
arithmetic mean (standard deviation)	1.2 (± 4.6)	1.6 (± 5.0)		

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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	233		
Units: millimetres squared (mm^2)				
arithmetic mean (standard deviation)	-5.4 (± 5.7)	-5.0 (± 6.4)		

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

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 ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	336		
Units: Percentage of participants				
number (not applicable)				
Adverse Event (AE)	88.3	89.3		
Serious AE (SAE)	24.0	27.7		
AE Leading to Withdrawal from Study Treatment	3.6	2.7		
AE of Special Interest (AESI)	4.8	6.8		

Statistical analyses

No statistical analyses for this end point

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

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 ≥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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	336		
Units: Percentage of participants				
number (not applicable)				
Study Eye: Adverse Event (AE)	55.0	56.5		
Study Eye: Serious AE (SAE)	4.2	3.9		
Study Eye: AE Leading to Withdrawal from Treatment	1.8	0.6		
Study Eye: Treatment-related AE	4.2	2.7		
Study Eye: Treatment-related SAE	1.2	0.0		
Study Eye: AE of Special Interest (AESI)	3.6	3.9		
Study Eye: AESI, Drop in VA Score ≥30 Letters	2.7	3.0		
Study Eye: AESI, Associated with Severe IOI	0.3	0.3		
StudyEye:AESI,Interv Req to Avoid Perm Vision Loss	0.6	0.6		
Fellow Eye: AE	39.3	44.3		
Fellow Eye: SAE	1.2	3.3		
Fellow Eye: AESI	1.2	3.0		
Fellow Eye: AESI, Drop in VA Score ≥30 Letters	0.9	2.1		
FellowEye:AESI,Inter Req to Avoid Perm Vision Loss	0.3	0.9		

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: Faricimab	Arm B: Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	333	336		
Units: Percentage of participants				
number (not applicable)				
Adverse Event (AE)	75.7	72.9		
Serious AE (SAE)	19.8	22.6		
AE Leading to Withdrawal from Study Treatment	1.8	2.1		
AE of Special Interest (AESI)	0.0	0.3		

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[49]

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: Faricimab			
Subject group type	Reporting group			
Number of subjects analysed	333			
Units: micrograms per millilitre (µg/mL)				
arithmetic mean (standard deviation)				
Baseline (n = 323)	0.0000 (± 0.0005)			
Week 4 (n = 321)	0.0288 (± 0.0194)			
Week 16 (n = 304)	0.0337 (± 0.0266)			
Week 20 (n = 296)	0.0044 (± 0.0062)			
Week 48 (n = 279)	0.0139 (± 0.0175)			
Week 76 (n = 258)	0.0057 (± 0.0109)			
Week 112 (n = 248)	0.0099 (± 0.0140)			

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[50]

End point description:

Anti-drug antibodies (ADAs) against fariciamb 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: Faricimab			
Subject group type	Reporting group			
Number of subjects analysed	330			
Units: Percentage of participants				
number (not applicable)				
Total Treatment-Emergent ADA-Positive	11.5			
Treatment-Induced ADA-Positive	11.2			
Treatment-Boosted ADA-Positive	0.3			

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 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).

Serious adverse events	Arm A: Faricimab	Arm B: Aflibercept	
Total subjects affected by serious adverse events			
subjects affected / exposed	80 / 333 (24.02%)	93 / 336 (27.68%)	
number of deaths (all causes)	13	7	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hair follicle tumour benign			

subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	2 / 333 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine carcinoma metastatic			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastric cancer recurrent			

subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cancer			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (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 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tracheal cancer			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			

subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colon neoplasm			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 333 (0.30%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			

subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Internal haemorrhage			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 333 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 333 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			

subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (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	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 333 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory distress			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 333 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal cyst			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (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	0 / 333 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus test positive			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (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			
Anaemia postoperative			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal abrasion			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthropod bite			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 333 (0.30%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Toxicity to various agents			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	2 / 333 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 333 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			

subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (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 left ventricular failure			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (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 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	5 / 333 (1.50%)	4 / 336 (1.19%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 333 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	3 / 333 (0.90%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Mitral valve prolapse			

subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis constrictive			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	2 / 333 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			

subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 333 (0.00%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 333 (0.60%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Somnolence			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 333 (0.30%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			

subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intensive care unit acquired weakness			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 333 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Age-related macular degeneration			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neovascular age-related macular degeneration			
subjects affected / exposed	1 / 333 (0.30%)	9 / 336 (2.68%)	
occurrences causally related to treatment / all	0 / 1	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	2 / 333 (0.60%)	5 / 336 (1.49%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal pigment epithelial tear			
subjects affected / exposed	2 / 333 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhegmatogenous retinal detachment			
subjects affected / exposed	1 / 333 (0.30%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subretinal fibrosis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uveitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal depigmentation			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			

subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (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	2 / 333 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tractional retinal detachment			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal degeneration			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry age-related macular degeneration			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lens dislocation			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 333 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 333 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (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	0 / 333 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 333 (0.00%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	2 / 333 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth cyst			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (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			

Chronic kidney disease			
subjects affected / exposed	2 / 333 (0.60%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	2 / 333 (0.60%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haematuria			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (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			
Osteoarthritis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scoliosis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteonecrosis of jaw			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	5 / 333 (1.50%)	4 / 336 (1.19%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 333 (1.80%)	5 / 336 (1.49%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pneumonia bacterial			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			

subjects affected / exposed	1 / 333 (0.30%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septic shock			
subjects affected / exposed	2 / 333 (0.60%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic bacterial infection			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral uveitis			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (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	2 / 333 (0.60%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural cellulitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	1 / 333 (0.30%)	1 / 336 (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 / 333 (0.90%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (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	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 333 (0.60%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin infection			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (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			
Dehydration			
subjects affected / exposed	0 / 333 (0.00%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	0 / 333 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Magnesium deficiency			
subjects affected / exposed	1 / 333 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A: Faricimab	Arm B: Aflibercept	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	211 / 333 (63.36%)	200 / 336 (59.52%)	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	17 / 333 (5.11%)	14 / 336 (4.17%)	
occurrences (all)	23	22	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	20 / 333 (6.01%)	20 / 336 (5.95%)	
occurrences (all)	29	24	
Vascular disorders			
Hypertension			
subjects affected / exposed	24 / 333 (7.21%)	13 / 336 (3.87%)	
occurrences (all)	25	13	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	36 / 333 (10.81%)	33 / 336 (9.82%)	
occurrences (all)	44	40	
Cataract			
subjects affected / exposed	27 / 333 (8.11%)	36 / 336 (10.71%)	
occurrences (all)	41	47	
Neovascular age-related macular degeneration			
subjects affected / exposed	65 / 333 (19.52%)	63 / 336 (18.75%)	
occurrences (all)	85	77	

Dry eye			
subjects affected / exposed	18 / 333 (5.41%)	24 / 336 (7.14%)	
occurrences (all)	27	42	
Eye pain			
subjects affected / exposed	14 / 333 (4.20%)	18 / 336 (5.36%)	
occurrences (all)	17	25	
Vitreous detachment			
subjects affected / exposed	19 / 333 (5.71%)	21 / 336 (6.25%)	
occurrences (all)	23	33	
Vitreous floaters			
subjects affected / exposed	23 / 333 (6.91%)	12 / 336 (3.57%)	
occurrences (all)	30	17	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	22 / 333 (6.61%)	19 / 336 (5.65%)	
occurrences (all)	25	20	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	23 / 333 (6.91%)	35 / 336 (10.42%)	
occurrences (all)	27	42	
Urinary tract infection			
subjects affected / exposed	26 / 333 (7.81%)	23 / 336 (6.85%)	
occurrences (all)	37	27	

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.; -Since patient recruitment was expected to take longer in Japan, a specific Japan enrollment plan was established. After the global enrollment phase of the study had been completed, additional patients could be enrolled in a Japan extension to ensure a total enrollment sufficient to support registration in Japan.; -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:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported