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 Macular Edema Secondary to Central Retinal or Hemiretinal Vein Occlusion

Summary

EudraCT number	2020-000441-13
Trial protocol	DE PT AT CZ HU FR PL IT
Global end of trial date	12 July 2023

Results information

Result version number	v1 (current)
This version publication date	26 July 2024
First version publication date	26 July 2024

Trial information

Trial identification

Sponsor protocol code	GR41986

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04740931
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche, Ltd.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4058
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	12 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective for this study is to evaluate the efficacy of faricimab 6 mg IVT Q4W compared with aflibercept 2 mg IVT Q4W on the basis of the change from baseline in BCVA at Week 24.

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	02 March 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 85
Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Brazil: 20
Country: Number of subjects enrolled	China: 57
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Japan: 49
Country: Number of subjects enrolled	Korea, Republic of: 42
Country: Number of subjects enrolled	Poland: 84
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Russian Federation: 25
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Spain: 22

Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	United Kingdom: 36
Country: Number of subjects enrolled	United States: 188
Worldwide total number of subjects	729
EEA total number of subjects	164

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)	320
From 65 to 84 years	377
85 years and over	32

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1004 patients were screened; 14 of these patients were rescreened and randomized in the study. A total of 274 patients failed screening due to not meeting the inclusion criteria. A total of 729 patients with C/HRVO were randomized 1:1 into the study: 366 to the faricimab Q4W arm and 363 to the aflibercept Q4W 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, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)

Arm description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections). In Part 2 (from Week 24 to Week 72), participants will receive faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure will be administered during study visits at which no faricimab treatment is administered (according to the PTI dosing regimen).

Arm type	Experimental
Investigational medicinal product name	Faricimab
Investigational medicinal product code	RO6867461
Other name	VABYSMO®
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Patients randomly assigned to Arm A received 6 mg faricimab intravitreal injections once every 4 weeks (Q4W) from Day 1 through Week 20 (6 injections) in Part 1 of the study. In Part 2 of the study, patients in Arm A switched from faricimab Q4W to receive 6 mg faricimab intravitreal injections according to a personalized treatment interval (PTI) dosing regimen from Week 24 through Week 68.

Arm title	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)

Arm description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections). In Part 2 (from Week 24 to Week 72), participants will receive faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure will be administered during study visits at which no faricimab treatment is administered (according to the PTI dosing regimen).

Arm type	Active comparator
Investigational medicinal product name	Faricimab
Investigational medicinal product code	RO6867461
Other name	VABYSMO®
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

In Part 2 of the study, patients in Arm B switched from aflibercept to receive 6 mg faricimab intravitreal

injections according to a personalized treatment interval (PTI) dosing regimen from Week 24 through Week 68.

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:

Patients randomly assigned to Arm B received 2 mg aflibercept intravitreal injections once every 4 weeks (Q4W) from Day 1 through Week 20 (6 injections) in Part 1 of the study.

Number of subjects in period 1	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)
Started	366	363
Received ≥1 Dose of Study Drug (Part 1)	365	361
Completed Part 1	360	353
Started Part 2	360	353
Completed	333	323
Not completed	33	40
Adverse event, serious fatal	5	3
Consent withdrawn by subject	11	15
Physician decision	2	2
Adverse event, non-fatal	6	6
Reason Not Specified	3	3
Non-compliance with study drug	3	-
Lost to follow-up	3	10
Protocol deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections). In Part 2 (from Week 24 to Week 72), participants will receive faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure will be administered during study visits at which no faricimab treatment is administered (according to the PTI dosing regimen).

Reporting group title	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections). In Part 2 (from Week 24 to Week 72), participants will receive faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure will be administered during study visits at which no faricimab treatment is administered (according to the PTI dosing regimen).

Reporting group values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)	Total
Number of subjects	366	363	729
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)	162	158	320
From 65-84 years	184	193	377
85 years and over	20	12	32
Age Continuous Units: Years			
arithmetic mean	65.6	64.7	
standard deviation	± 13.1	± 13.3	-
Sex: Female, Male Units: Participants			
Female	173	163	336
Male	193	200	393
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	3	5
Asian	89	88	177
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	10	13	23
White	243	253	496

More than one race	1	0	1
Unknown or Not Reported	21	5	26
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	66	73	139
Not Hispanic or Latino	286	283	569
Unknown or Not Reported	14	7	21
Region of Enrollment Units: Subjects			
Rest of World	187	187	374
USA and Canada	95	93	188
Asia	84	83	167
Number of Participants by the Eye (Left or Right) Chosen as the Study Eye Units: Subjects			
Left Eye	180	181	361
Right Eye	186	182	368
Number of Participants by the BCVA Letter Score Categories in the Study Eye Units: Subjects			
≤34 Letters (20/200 or Worse)	79	80	159
>34 Letters to <55 Letters	106	105	211
≥55 Letters (20/80 or Better)	181	178	359
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye Units: ETDRS Letters			
arithmetic mean	50.25	50.71	
standard deviation	± 16.25	± 16.34	-

Subject analysis sets

Subject analysis set title	Arm A: Faricimab Q4W (Part 1)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	Arm B: Aflibercept Q4W (Part 1)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham

procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W (Part 1)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	Arm B: Aflibercept Q4W (Part 1)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	All Faricimab Participants
Subject analysis set type	Safety analysis

Subject analysis set description:

This immunogenicity analysis group represents all participants with an evaluable ADA sample. At baseline, evaluable participants were those with an ADA sample prior to faricimab injection, including those who did not receive study treatment; post-baseline, evaluable participants were those with an ADA sample after having received at least one dose of faricimab.

Reporting group values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Number of subjects	366	363	340
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years			
arithmetic mean	16.9	17.3	
standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
Region of Enrollment Units: Subjects			
Rest of World USA and Canada Asia			
Number of Participants by the Eye (Left or Right) Chosen as the Study Eye Units: Subjects			

Left Eye			
Right Eye			
Number of Participants by the BCVA Letter Score Categories in the Study Eye			
Units: Subjects			
≤34 Letters (20/200 or Worse)			
>34 Letters to <55 Letters			
≥55 Letters (20/80 or Better)			
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye			
Units: ETDRS Letters			
arithmetic mean	16.9	17.3	
standard deviation	±	±	±

Reporting group values	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Number of subjects	331	366	363
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			

Region of Enrollment Units: Subjects			
Rest of World USA and Canada Asia			
Number of Participants by the Eye (Left or Right) Chosen as the Study Eye Units: Subjects			
Left Eye Right Eye			
Number of Participants by the BCVA Letter Score Categories in the Study Eye Units: Subjects			
≤34 Letters (20/200 or Worse) >34 Letters to <55 Letters ≥55 Letters (20/80 or Better)			
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye Units: ETDRS Letters arithmetic mean standard deviation	±	±	±

Reporting group values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Number of subjects	330	315	359
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	5.0 ±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American			

White			
More than one race			
Unknown or Not Reported			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			
Region of Enrollment			
Units: Subjects			
Rest of World			
USA and Canada			
Asia			
Number of Participants by the Eye (Left or Right) Chosen as the Study Eye			
Units: Subjects			
Left Eye			
Right Eye			
Number of Participants by the BCVA Letter Score Categories in the Study Eye			
Units: Subjects			
≤34 Letters (20/200 or Worse)			
>34 Letters to <55 Letters			
≥55 Letters (20/80 or Better)			
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye			
Units: ETDRS Letters			
arithmetic mean			5.0
standard deviation	±	±	±

Reporting group values	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)
Number of subjects	342	365	361
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Years			
arithmetic mean	4.0		
standard deviation	±	±	±
Sex: Female, Male			
Units: Participants			
Female			

Male			

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
Region of Enrollment Units: Subjects			
Rest of World USA and Canada Asia			
Number of Participants by the Eye (Left or Right) Chosen as the Study Eye Units: Subjects			
Left Eye Right Eye			
Number of Participants by the BCVA Letter Score Categories in the Study Eye Units: Subjects			
≤34 Letters (20/200 or Worse) >34 Letters to <55 Letters ≥55 Letters (20/80 or Better)			
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye Units: ETDRS Letters arithmetic mean standard deviation	 4.0 ±	 ±	 ±

Reporting group values	All Faricimab Participants		
Number of subjects	708		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years)			

From 65-84 years			
85 years and over			

Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	±		
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			
Region of Enrollment			
Units: Subjects			
Rest of World			
USA and Canada			
Asia			
Number of Participants by the Eye (Left or Right) Chosen as the Study Eye			
Units: Subjects			
Left Eye			
Right Eye			
Number of Participants by the BCVA Letter Score Categories in the Study Eye			
Units: Subjects			
≤34 Letters (20/200 or Worse)			
>34 Letters to <55 Letters			
≥55 Letters (20/80 or Better)			
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye			
Units: ETDRS Letters			
arithmetic mean			
standard deviation	±		

End points reporting groups

Reporting group title	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections). In Part 2 (from Week 24 to Week 72), participants will receive faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure will be administered during study visits at which no faricimab treatment is administered (according to the PTI dosing regimen).

Reporting group title	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections). In Part 2 (from Week 24 to Week 72), participants will receive faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure will be administered during study visits at which no faricimab treatment is administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W (Part 1)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	Arm B: Aflibercept Q4W (Part 1)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

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Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered

(according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Subject analysis set title	Arm A: Faricimab Q4W (Part 1)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	Arm B: Aflibercept Q4W (Part 1)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Subject analysis set title	All Faricimab Participants
Subject analysis set type	Safety analysis

Subject analysis set description:

This immunogenicity analysis group represents all participants with an evaluable ADA sample. At baseline, evaluable participants were those with an ADA sample prior to faricimab injection, including those who did not receive study treatment; post-baseline, evaluable participants were those with an ADA sample after having received at least one dose of faricimab.

Primary: Part 1: Change from Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye at Week 24

End point title	Part 1: Change from Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye at Week 24

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 included the categorical covariates of treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), and randomization stratification factors

[baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)] as fixed effects. An unstructured covariance structure was used. Missing data were implicitly imputed by MMRM model assuming missing at random. Treatment policy strategy (i.e., all observed values used) was applied to all intercurrent events (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). 95% CI is a rounding of 95.03% CI.

End point type	Primary

End point timeframe:

From Baseline through Week 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)	16.9 (15.4 to 18.3)	17.3 (15.9 to 18.8)		

Statistical analyses

Statistical analysis title	BCVA Superiority

Statistical analysis description:

The final sample size provided >80% power for a 3.5-letter superiority assessment of faricimab over aflibercept (at a two-sided 0.0497 significance level).

Comparison groups	Arm A: Faricimab Q4W (Part 1) v Arm B: Aflibercept Q4W (Part 1)
Number of subjects included in analysis	729
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6715 [1]
Method	Mixed Model of Repeated Measures
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	1.04

Notes:

[1] - Tested at a two-sided p<0.0497 significance level.

Statistical analysis title	BCVA Non-inferiority

Statistical analysis description:

The null hypothesis, H0: μ(faricimab) − μ(aflibercept) ≤−4 letters; the alternative hypothesis, Ha: μ(faricimab) − μ(aflibercept) >−4 letters. The final sample size provided >90% power for the non-inferiority assessment (at a one-sided 0.02485 significance level).

Comparison groups	Arm A: Faricimab Q4W (Part 1) v Arm B: Aflibercept Q4W (Part

	1)
Number of subjects included in analysis	729
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	1.04

Notes:

[2] - If the lower bound of a two-sided 95% 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: Part 1: Change from Baseline in BCVA in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Change from Baseline in BCVA in the Study Eye at Specified Timepoints Through Week 24

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 included the categorical covariates of treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), and randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)] as fixed effects. An unstructured covariance structure was used. Missing data were implicitly imputed by MMRM model assuming missing at random. Treatment policy strategy (i.e., all observed values used) was applied to all intercurrent events (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 4	13.5 (12.5 to 14.6)	14.3 (13.2 to 15.4)		
Week 8	15.5 (14.4 to 16.7)	16.5 (15.3 to 17.7)		
Week 12	16.9 (15.7 to 18.2)	17.1 (15.8 to 18.4)		
Week 16	16.8 (15.4 to 18.1)	17.5 (16.2 to 18.9)		
Week 20	17.0 (15.6 to 18.3)	17.2 (15.8 to 18.5)		

Week 24	16.9 (15.4 to 18.3)	17.3 (15.9 to 18.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline in the Study Eye at Week 24

End point title	Part 1: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline in the Study Eye at Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

From Baseline through Week 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)	56.6 (51.7 to 61.5)	58.1 (53.3 to 62.9)		

Statistical analyses

Statistical analysis title	Gaining ≥15 Letters
Comparison groups	Arm A: Faricimab Q4W (Part 1) v Arm B: Aflibercept Q4W (Part 1)
Number of subjects included in analysis	729
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	5.3

Secondary: Part 1: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	41.5 (36.7 to 46.3)	45.4 (40.7 to 50.2)		
Week 8	51.1 (46.3 to 55.9)	53.7 (48.9 to 58.5)		
Week 12	54.6 (49.8 to 59.4)	55.1 (50.3 to 59.9)		
Week 16	57.7 (52.8 to 62.5)	59.5 (54.7 to 64.3)		
Week 20	56.6 (51.7 to 61.4)	57.8 (53.0 to 62.6)		
Week 24	56.6 (51.7 to 61.5)	58.1 (53.3 to 62.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Gaining ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Gaining ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	60.9 (56.0 to 65.8)	62.3 (57.6 to 66.9)		
Week 8	69.1 (64.5 to 73.7)	72.8 (68.3 to 77.2)		
Week 12	73.2 (68.8 to 77.7)	74.7 (70.3 to 79.0)		
Week 16	73.5 (69.1 to 78.0)	75.8 (71.4 to 80.1)		
Week 20	72.4 (68.0 to 76.9)	74.1 (69.7 to 78.5)		
Week 24	72.2 (67.7 to 76.6)	73.3 (68.8 to 77.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Gaining ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Gaining ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights

stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	83.1 (79.3 to 86.9)	83.5 (79.7 to 87.2)		
Week 8	85.2 (81.7 to 88.8)	86.8 (83.3 to 90.2)		
Week 12	87.4 (84.1 to 90.8)	87.1 (83.7 to 90.5)		
Week 16	86.3 (82.9 to 89.8)	88.7 (85.5 to 92.0)		
Week 20	84.1 (80.5 to 87.8)	86.5 (83.0 to 90.0)		
Week 24	85.3 (81.8 to 88.8)	84.6 (80.9 to 88.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Gaining >0 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Gaining >0 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	92.1 (89.4 to 94.8)	95.6 (93.5 to 97.7)		
Week 8	92.1 (89.4 to 94.8)	94.8 (92.5 to 97.0)		
Week 12	93.2 (90.6 to 95.7)	92.6 (89.9 to 95.2)		
Week 16	92.6 (90.0 to 95.3)	92.0 (89.3 to 94.8)		
Week 20	90.5 (87.5 to 93.4)	91.4 (88.6 to 94.3)		
Week 24	90.5 (87.5 to 93.4)	89.2 (86.1 to 92.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	98.4 (97.1 to 99.7)	98.9 (97.8 to 100.0)		
Week 8	98.1 (96.7 to 99.5)	98.1 (96.7 to 99.5)		
Week 12	98.6 (97.5 to 99.8)	97.5 (95.9 to 99.1)		
Week 16	97.3 (95.6 to 98.9)	97.0 (95.2 to 98.7)		
Week 20	97.0 (95.3 to 98.7)	96.7 (94.9 to 98.5)		
Week 24	96.2 (94.3 to 98.1)	96.7 (94.9 to 98.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	98.1 (96.7 to 99.5)	98.6 (97.4 to 99.8)		

Week 8	97.5 (96.0 to 99.1)	97.5 (95.9 to 99.1)		
Week 12	97.8 (96.3 to 99.3)	97.0 (95.2 to 98.7)		
Week 16	95.9 (93.9 to 97.9)	96.1 (94.2 to 98.1)		
Week 20	96.7 (94.9 to 98.5)	96.1 (94.2 to 98.1)		
Week 24	95.1 (92.9 to 97.3)	95.9 (93.8 to 97.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Achieving ≥84 Letters in BCVA (20/20 Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Achieving ≥84 Letters in BCVA (20/20 Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	6.0 (3.6 to 8.4)	4.7 (2.6 to 6.8)		
Week 8	8.7 (5.9 to 11.5)	10.2 (7.2 to 13.2)		
Week 12	10.9 (7.8 to 14.0)	11.9 (8.7 to 15.0)		
Week 16	11.5 (8.4 to 14.6)	14.1 (10.7 to 17.5)		
Week 20	14.2 (10.9 to 17.6)	14.9 (11.4 to 18.3)		
Week 24	14.5 (11.0 to 17.9)	15.2 (11.7 to 18.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	97.0 (95.3 to 98.7)	98.1 (96.7 to 99.5)		
Week 8	96.2 (94.2 to 98.1)	96.4 (94.5 to 98.3)		
Week 12	95.9 (93.9 to 97.9)	96.1 (94.2 to 98.1)		
Week 16	95.4 (93.2 to 97.5)	94.8 (92.5 to 97.0)		
Week 20	94.8 (92.6 to 97.1)	93.9 (91.5 to 96.4)		
Week 24	94.0 (91.6 to 96.4)	93.7 (91.2 to 96.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants Achieving ≥69 Letters in BCVA (20/40 or Better Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants Achieving ≥69 Letters in BCVA (20/40 or Better Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	45.0 (41.0 to 49.1)	46.1 (41.9 to 50.2)		
Week 8	48.6 (44.3 to 52.8)	54.6 (50.5 to 58.7)		
Week 12	54.9 (50.8 to 58.9)	55.7 (51.4 to 60.0)		
Week 16	54.9 (50.6 to 59.1)	59.3 (55.2 to 63.4)		
Week 20	54.1 (49.7 to 58.4)	57.6 (53.4 to 61.8)		
Week 24	55.7 (51.3 to 60.0)	59.0 (54.5 to 63.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants with ≤38 Letters in BCVA (20/200 or Worse Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants with ≤38 Letters in BCVA (20/200 or Worse Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 24

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (>38 and ≤38 letters) and region (U.S. and Canada, Asia, and rest of the world). All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	10.0 (7.3 to 12.8)	8.6 (6.1 to 11.1)		
Week 8	8.2 (5.5 to 10.8)	7.0 (4.6 to 9.4)		
Week 12	7.3 (4.9 to 9.8)	6.4 (4.0 to 8.8)		
Week 16	7.8 (5.3 to 10.4)	6.2 (3.8 to 8.5)		
Week 20	8.4 (5.7 to 11.0)	6.4 (4.0 to 8.8)		
Week 24	10.1 (7.1 to 13.0)	7.5 (4.9 to 10.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change from Baseline in Central Subfield Thickness in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Change from Baseline in Central Subfield Thickness in the Study Eye at Specified Timepoints Through Week 24

End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and the Bruch's membrane (BM) using optical coherence tomography (OCT), as assessed by the central reading center. The Mixed Model of Repeated Measures (MMRM) analysis included the categorical covariates of treatment arm, visit, visit-by-treatment arm interaction, baseline CST (continuous), and randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)] as fixed effects. An unstructured covariance structure was used. Missing data were implicitly imputed by MMRM model assuming missing at random. Treatment policy strategy (i.e., all observed values used) was applied to all intercurrent events (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: microns				
arithmetic mean (confidence interval 95%)				
Week 4	-420.8 (-429.2 to -412.5)	-417.3 (-425.6 to -409.0)		
Week 8	-444.2 (-452.7 to -435.7)	-437.5 (-446.1 to -429.0)		
Week 12	-451.0 (-460.6 to -441.5)	-442.5 (-452.1 to -433.0)		
Week 16	-452.5 (-461.8 to -443.1)	-445.2 (-454.7 to -435.8)		
Week 20	-459.4 (-467.8 to -451.0)	-445.1 (-453.6 to -436.6)		
Week 24	-461.6 (-471.4 to -451.9)	-448.8 (-458.6 to -439.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants with Absence of Macular Edema in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants with Absence of Macular Edema in the Study Eye at Specified Timepoints Through Week 24

End point description:

Absence of diabetic macular edema was defined as achieving a central subfield thickness of <325 microns in the study eye. Central subfield thickness was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	83.8 (80.2 to 87.5)	82.4 (78.5 to 86.2)		
Week 8	92.6 (90.0 to 95.2)	91.2 (88.3 to 94.1)		
Week 12	93.4 (90.9 to 95.9)	91.5 (88.6 to 94.3)		
Week 16	94.5 (92.2 to 96.8)	92.8 (90.2 to 95.5)		
Week 20	94.8 (92.6 to 97.1)	93.1 (90.5 to 95.7)		
Week 24	93.7 (91.2 to 96.2)	92.0 (89.2 to 94.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye at Specified Timepoints Through Week 24

End point description:

Intraretinal fluid was measured in the study eye using optical coherence tomography (OCT) in the central subfield (center 1 mm) by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	45.5 (40.6 to 50.5)	40.3 (35.6 to 45.0)		
Week 8	63.1 (58.3 to 68.0)	61.7 (56.9 to 66.6)		

Week 12	53.2 (48.3 to 58.2)	51.0 (46.2 to 55.9)		
Week 16	55.4 (50.5 to 60.3)	51.9 (46.8 to 56.9)		
Week 20	59.0 (54.0 to 63.9)	56.5 (51.6 to 61.5)		
Week 24	76.2 (71.9 to 80.5)	70.8 (66.2 to 75.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants with Absence of Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants with Absence of Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 24

End point description:

Subretinal fluid was measured in the study eye using optical coherence tomography (OCT) in the central subfield (center 1 mm) by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	66.1 (61.4 to 70.8)	65.0 (60.3 to 69.7)		
Week 8	89.6 (86.5 to 92.6)	90.1 (87.0 to 93.1)		
Week 12	94.0 (91.6 to 96.4)	93.9 (91.5 to 96.4)		
Week 16	95.3 (93.2 to 97.5)	95.6 (93.5 to 97.7)		
Week 20	95.9 (93.9 to 97.9)	94.5 (92.2 to 96.8)		
Week 24	96.4 (94.6 to 98.3)	93.4 (90.8 to 95.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Percentage of Participants with Absence of Intraretinal Fluid and Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 24

End point title	Part 1: Percentage of Participants with Absence of Intraretinal Fluid and Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 24

End point description:

Intraretinal fluid and subretinal fluid were measured in the study eye using optical coherence tomography (OCT) in the central subfield (center 1 mm) by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	33.0 (28.3 to 37.6)	29.3 (24.9 to 33.7)		
Week 8	59.3 (54.4 to 64.1)	59.3 (54.3 to 64.2)		
Week 12	52.7 (47.7 to 57.6)	50.2 (45.3 to 55.1)		
Week 16	54.9 (49.9 to 59.8)	51.3 (46.3 to 56.3)		
Week 20	58.2 (53.2 to 63.1)	55.4 (50.5 to 60.4)		
Week 24	75.1 (70.8 to 79.5)	68.6 (63.8 to 73.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Change from Baseline in National Eye Institute 25-Item Visual Functioning Questionnaire (NEI VFQ-25) Composite Score at Week 24

End point title	Part 1: Change from Baseline in National Eye Institute 25-Item Visual Functioning Questionnaire (NEI VFQ-25) Composite Score at Week 24

End point description:

The NEI VFQ-25 captures a patient's perception of vision-related functioning and vision-related quality of life. The core measure includes 25 items that comprise 11 vision-related subscales and 1 item on general health. The composite score ranges from 0 to 100, with higher scores indicating better vision-related functioning. For the ANCOVA analysis, the model uses the non-missing change from baseline in BCVA at Weeks 24 as the response variables adjusted for the treatment group, baseline NEI VFQ-25 Composite Score (continuous), baseline BCVA score (≥55 and ≤54 letters) and region (U.S. and Canada, Asia, and the rest of the world). Observed NEI VFQ-25 assessments were used regardless of the occurrence of intercurrent events. Missing data were not imputed. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	339	330		
Units: score on a scale				
arithmetic mean (confidence interval 95%)	6.9 (5.8 to 8.0)	8.1 (7.0 to 9.2)		

Statistical analyses

Statistical analysis title	NEI VFQ-25 at Week 24
Comparison groups	Arm A: Faricimab Q4W (Part 1) v Arm B: Aflibercept Q4W (Part 1)
Number of subjects included in analysis	669
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Adjusted Means
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.77

Secondary: Parts 1 and 2: Change from Baseline in BCVA in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Change from Baseline in BCVA in the Study Eye at Specified Timepoints Through Week 72

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 included the categorical covariates of treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), and randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)] as fixed effects. An unstructured covariance structure was used. Missing data were implicitly imputed by MMRM model assuming missing at random. Treatment policy strategy (i.e., all observed values used) was applied to all intercurrent events (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 4	13.6 (12.5 to 14.6)	14.3 (13.3 to 15.4)		
Week 8	15.6 (14.4 to 16.8)	16.5 (15.4 to 17.7)		
Week 12	17.0 (15.7 to 18.2)	17.2 (15.9 to 18.4)		
Week 16	16.8 (15.5 to 18.1)	17.6 (16.2 to 18.9)		
Week 20	17.0 (15.7 to 18.4)	17.3 (15.9 to 18.6)		
Week 24	16.9 (15.5 to 18.3)	17.3 (15.9 to 18.8)		
Week 28	16.0 (14.5 to 17.5)	16.0 (14.4 to 17.5)		
Week 32	17.2 (15.7 to 18.7)	17.5 (16.0 to 19.0)		
Week 36	17.0 (15.5 to 18.5)	17.5 (15.9 to 19.0)		
Week 40	15.8 (14.2 to 17.5)	16.2 (14.5 to 17.9)		
Week 44	16.5 (14.9 to 18.2)	17.3 (15.7 to 19.0)		
Week 48	16.9 (15.2 to 18.5)	17.6 (15.9 to 19.3)		
Week 52	16.4 (14.8 to 18.1)	17.8 (16.2 to 19.5)		
Week 56	16.0 (14.3 to 17.7)	16.9 (15.2 to 18.6)		
Week 60	16.9 (15.2 to 18.6)	17.3 (15.6 to 19.0)		
Week 64	16.8 (15.1 to 18.5)	17.2 (15.5 to 18.9)		
Week 68	16.9 (15.2 to 18.7)	17.0 (15.2 to 18.7)		
Week 72	16.9 (15.1 to 18.6)	17.1 (15.3 to 18.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	41.5 (36.7 to 46.3)	45.2 (40.4 to 49.9)		
Week 8	51.1 (46.3 to 55.9)	53.7 (48.9 to 58.5)		
Week 12	54.6 (49.8 to 59.4)	55.1 (50.3 to 59.9)		
Week 16	57.7 (52.8 to 62.5)	59.5 (54.7 to 64.3)		
Week 20	56.6 (51.7 to 61.4)	57.8 (53.0 to 62.6)		
Week 24	56.6 (51.7 to 61.5)	58.1 (53.3 to 62.9)		
Week 28	53.3 (48.4 to 58.2)	54.8 (50.0 to 59.6)		
Week 32	60.9 (56.1 to 65.8)	57.6 (52.7 to 62.4)		

Week 36	58.2 (53.3 to 63.1)	58.9 (54.2 to 63.7)		
Week 40	56.6 (51.7 to 61.4)	55.9 (51.1 to 60.7)		
Week 44	55.7 (50.9 to 60.6)	57.3 (52.5 to 62.1)		
Week 48	58.8 (53.9 to 63.6)	58.1 (53.3 to 62.9)		
Week 52	57.6 (52.7 to 62.5)	58.7 (53.8 to 63.5)		
Week 56	56.3 (51.3 to 61.2)	57.3 (52.5 to 62.2)		
Week 60	58.2 (53.3 to 63.1)	59.0 (54.1 to 63.8)		
Week 64	57.1 (52.3 to 61.9)	59.5 (54.7 to 64.3)		
Week 68	56.8 (52.0 to 61.6)	59.8 (54.9 to 64.6)		
Week 72	58.7 (53.9 to 63.6)	60.0 (55.2 to 64.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Gaining ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Gaining ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				

Week 4	60.9 (56.0 to 65.8)	62.3 (57.6 to 66.9)		
Week 8	69.1 (64.5 to 73.7)	72.8 (68.3 to 77.2)		
Week 12	73.2 (68.8 to 77.7)	74.7 (70.3 to 79.0)		
Week 16	73.5 (69.1 to 78.0)	75.8 (71.4 to 80.1)		
Week 20	72.4 (68.0 to 76.9)	74.1 (69.7 to 78.5)		
Week 24	72.2 (67.7 to 76.6)	73.3 (68.8 to 77.7)		
Week 28	69.7 (65.1 to 74.3)	70.5 (66.0 to 75.1)		
Week 32	73.0 (68.5 to 77.4)	74.4 (70.0 to 78.8)		
Week 36	73.8 (69.3 to 78.2)	74.9 (70.6 to 79.3)		
Week 40	71.0 (66.5 to 75.6)	73.0 (68.6 to 77.5)		
Week 44	71.6 (67.1 to 76.1)	74.1 (69.7 to 78.5)		
Week 48	71.9 (67.3 to 76.4)	75.5 (71.1 to 79.9)		
Week 52	71.0 (66.4 to 75.6)	73.8 (69.4 to 78.3)		
Week 56	70.8 (66.2 to 75.3)	72.2 (67.6 to 76.7)		
Week 60	72.7 (68.2 to 77.2)	72.5 (67.9 to 77.0)		
Week 64	72.4 (67.9 to 76.9)	71.6 (67.0 to 76.2)		
Week 68	72.1 (67.7 to 76.6)	70.5 (65.9 to 75.1)		
Week 72	71.6 (67.1 to 76.1)	73.0 (68.5 to 77.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Gaining ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Gaining ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	83.1 (79.3 to 86.9)	83.5 (79.7 to 87.2)		
Week 8	85.2 (81.7 to 88.8)	86.8 (83.3 to 90.2)		
Week 12	87.4 (84.1 to 90.8)	87.1 (83.7 to 90.5)		
Week 16	86.3 (82.9 to 89.8)	88.7 (85.5 to 92.0)		
Week 20	84.1 (80.5 to 87.8)	86.5 (83.0 to 90.0)		
Week 24	85.3 (81.8 to 88.8)	84.6 (80.9 to 88.2)		
Week 28	81.7 (77.8 to 85.6)	84.0 (80.3 to 87.7)		
Week 32	84.2 (80.5 to 87.8)	87.3 (83.9 to 90.7)		
Week 36	84.7 (81.1 to 88.3)	85.7 (82.1 to 89.3)		
Week 40	82.3 (78.4 to 86.1)	84.3 (80.6 to 88.0)		
Week 44	82.8 (79.0 to 86.6)	84.9 (81.2 to 88.5)		
Week 48	83.6 (79.9 to 87.3)	83.7 (80.0 to 87.5)		
Week 52	80.9 (76.9 to 84.8)	84.0 (80.3 to 87.8)		
Week 56	79.2 (75.2 to 83.3)	81.5 (77.6 to 85.5)		
Week 60	82.8 (79.0 to 86.6)	81.6 (77.6 to 85.5)		
Week 64	80.6 (76.6 to 84.6)	81.5 (77.6 to 85.5)		
Week 68	83.3 (79.6 to 87.1)	80.2 (76.1 to 84.2)		
Week 72	83.6 (79.9 to 87.3)	79.6 (75.5 to 83.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Gaining >0 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Gaining >0 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	92.1 (89.4 to 94.8)	95.6 (93.5 to 97.7)		
Week 8	92.1 (89.4 to 94.8)	94.8 (92.5 to 97.0)		
Week 12	93.2 (90.6 to 95.7)	92.6 (89.9 to 95.2)		
Week 16	92.6 (90.0 to 95.3)	92.0 (89.3 to 94.8)		
Week 20	90.5 (87.5 to 93.4)	91.4 (88.6 to 94.3)		
Week 24	90.5 (87.5 to 93.4)	89.2 (86.1 to 92.4)		
Week 28	88.0 (84.7 to 91.3)	88.4 (85.2 to 91.7)		
Week 32	89.4 (86.2 to 92.5)	92.0 (89.2 to 94.8)		
Week 36	89.9 (86.9 to 93.0)	90.1 (87.0 to 93.1)		
Week 40	87.7 (84.5 to 91.0)	88.7 (85.5 to 91.9)		
Week 44	88.5 (85.3 to 91.7)	89.2 (86.1 to 92.4)		
Week 48	88.5 (85.3 to 91.7)	88.7 (85.5 to 91.9)		
Week 52	85.8 (82.2 to 89.3)	89.0 (85.8 to 92.2)		
Week 56	85.8 (82.3 to 89.3)	87.3 (83.9 to 90.7)		
Week 60	86.6 (83.2 to 90.0)	87.3 (83.9 to 90.7)		

Week 64	86.1 (82.6 to 89.6)	86.2 (82.7 to 89.7)		
Week 68	87.4 (84.1 to 90.8)	85.4 (81.8 to 89.0)		
Week 72	86.6 (83.2 to 90.1)	85.7 (82.1 to 89.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	98.4 (97.1 to 99.7)	98.9 (97.8 to 100.0)		
Week 8	98.1 (96.7 to 99.5)	98.1 (96.7 to 99.5)		
Week 12	98.6 (97.5 to 99.8)	97.5 (95.9 to 99.1)		
Week 16	97.3 (95.6 to 98.9)	97.0 (95.2 to 98.7)		
Week 20	97.0 (95.3 to 98.7)	96.7 (94.9 to 98.5)		
Week 24	96.2 (94.3 to 98.1)	96.7 (94.9 to 98.5)		
Week 28	95.6 (93.6 to 97.7)	94.2 (91.8 to 96.6)		

Week 32	95.4 (93.3 to 97.5)	96.1 (94.2 to 98.1)		
Week 36	95.4 (93.3 to 97.5)	95.9 (93.8 to 97.9)		
Week 40	94.0 (91.6 to 96.4)	95.9 (93.8 to 97.9)		
Week 44	94.0 (91.6 to 96.4)	95.6 (93.5 to 97.7)		
Week 48	94.0 (91.6 to 96.4)	95.6 (93.5 to 97.7)		
Week 52	94.6 (92.3 to 96.8)	96.7 (94.9 to 98.5)		
Week 56	95.1 (92.9 to 97.3)	95.6 (93.5 to 97.7)		
Week 60	93.5 (91.0 to 96.0)	95.3 (93.2 to 97.5)		
Week 64	94.0 (91.6 to 96.4)	94.8 (92.5 to 97.0)		
Week 68	93.5 (90.9 to 96.0)	95.9 (93.8 to 97.9)		
Week 72	93.2 (90.6 to 95.7)	95.0 (92.8 to 97.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				

number (confidence interval 95%)				
Week 4	98.1 (96.7 to 99.5)	98.6 (97.4 to 99.8)		
Week 8	97.5 (96.0 to 99.1)	97.5 (95.9 to 99.1)		
Week 12	97.8 (96.3 to 99.3)	97.0 (95.2 to 98.7)		
Week 16	95.9 (93.9 to 97.9)	96.1 (94.2 to 98.1)		
Week 20	96.7 (94.9 to 98.5)	96.1 (94.2 to 98.1)		
Week 24	95.1 (92.9 to 97.3)	95.9 (93.8 to 97.9)		
Week 28	94.6 (92.3 to 96.9)	93.4 (90.9 to 95.9)		
Week 32	94.3 (91.9 to 96.6)	95.9 (93.8 to 97.9)		
Week 36	94.3 (91.9 to 96.6)	95.0 (92.8 to 97.3)		
Week 40	92.9 (90.3 to 95.5)	93.9 (91.5 to 96.4)		
Week 44	93.2 (90.7 to 95.7)	94.5 (92.2 to 96.8)		
Week 48	92.4 (89.7 to 95.0)	93.9 (91.5 to 96.4)		
Week 52	92.9 (90.3 to 95.5)	95.0 (92.8 to 97.2)		
Week 56	91.3 (88.4 to 94.1)	93.6 (91.2 to 96.1)		
Week 60	92.1 (89.4 to 94.8)	94.5 (92.2 to 96.8)		
Week 64	92.9 (90.3 to 95.5)	93.9 (91.5 to 96.4)		
Week 68	92.6 (90.0 to 95.3)	94.2 (91.8 to 96.6)		
Week 72	92.6 (90.0 to 95.3)	93.7 (91.2 to 96.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA from Baseline in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	97.0 (95.3 to 98.7)	98.1 (96.7 to 99.5)		
Week 8	96.2 (94.2 to 98.1)	96.4 (94.5 to 98.3)		
Week 12	95.9 (93.9 to 97.9)	96.1 (94.2 to 98.1)		
Week 16	95.4 (93.2 to 97.5)	94.8 (92.5 to 97.0)		
Week 20	94.8 (92.6 to 97.1)	93.9 (91.5 to 96.4)		
Week 24	94.0 (91.6 to 96.4)	93.7 (91.2 to 96.1)		
Week 28	92.4 (89.7 to 95.1)	91.7 (88.9 to 94.5)		
Week 32	91.3 (88.4 to 94.1)	94.8 (92.5 to 97.0)		
Week 36	92.7 (90.0 to 95.3)	94.2 (91.8 to 96.6)		
Week 40	91.0 (88.1 to 93.9)	92.6 (89.9 to 95.2)		
Week 44	90.7 (87.8 to 93.6)	92.8 (90.2 to 95.4)		
Week 48	91.0 (88.1 to 93.9)	92.6 (89.9 to 95.2)		
Week 52	90.5 (87.5 to 93.4)	93.4 (90.9 to 95.9)		
Week 56	88.5 (85.3 to 91.7)	91.4 (88.6 to 94.3)		
Week 60	90.5 (87.5 to 93.4)	92.3 (89.6 to 95.0)		
Week 64	90.7 (87.8 to 93.7)	91.2 (88.3 to 94.1)		
Week 68	89.6 (86.6 to 92.7)	91.7 (88.9 to 94.5)		
Week 72	90.5 (87.5 to 93.4)	90.6 (87.7 to 93.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Achieving ≥84 Letters in BCVA (20/20 Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Achieving ≥84 Letters in BCVA (20/20 Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	6.0 (3.6 to 8.4)	4.7 (2.6 to 6.8)		
Week 8	8.7 (5.9 to 11.5)	10.2 (7.2 to 13.2)		
Week 12	10.9 (7.8 to 14.0)	11.9 (8.7 to 15.0)		
Week 16	11.5 (8.4 to 14.6)	14.1 (10.7 to 17.5)		
Week 20	14.2 (10.9 to 17.6)	14.9 (11.4 to 18.3)		
Week 24	14.5 (11.0 to 17.9)	15.2 (11.7 to 18.7)		
Week 28	9.8 (6.9 to 12.8)	12.7 (9.5 to 15.9)		
Week 32	13.4 (10.0 to 16.7)	14.9 (11.4 to 18.3)		
Week 36	15.3 (11.8 to 18.8)	14.9 (11.5 to 18.3)		
Week 40	14.8 (11.3 to 18.2)	12.4 (9.2 to 15.7)		
Week 44	15.5 (12.0 to 19.1)	14.1 (10.7 to 17.5)		
Week 48	15.0 (11.6 to 18.5)	14.6 (11.2 to 18.0)		
Week 52	16.7 (13.0 to 20.3)	14.9 (11.4 to 18.4)		
Week 56	14.8 (11.3 to 18.2)	15.5 (12.0 to 18.9)		

Week 60	15.8 (12.3 to 19.4)	16.3 (12.7 to 19.9)		
Week 64	16.1 (12.5 to 19.8)	15.7 (12.2 to 19.3)		
Week 68	15.3 (11.8 to 18.9)	15.2 (11.7 to 18.7)		
Week 72	15.3 (11.8 to 18.8)	14.4 (11.0 to 17.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants Achieving ≥69 Letters in BCVA (20/40 or Better Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants Achieving ≥69 Letters in BCVA (20/40 or Better Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	45.0 (41.0 to 49.1)	46.1 (41.9 to 50.2)		
Week 8	48.6 (44.3 to 52.8)	54.6 (50.5 to 58.7)		
Week 12	54.9 (50.8 to 58.9)	55.7 (51.4 to 60.0)		
Week 16	54.9 (50.6 to 59.1)	59.3 (55.2 to 63.4)		
Week 20	54.1 (49.7 to 58.4)	57.6 (53.4 to 61.8)		
Week 24	55.7 (51.3 to 60.0)	59.0 (54.5 to 63.4)		

Week 28	53.2 (48.8 to 57.7)	56.2 (51.8 to 60.7)		
Week 32	56.0 (51.6 to 60.4)	60.4 (56.1 to 64.6)		
Week 36	53.8 (49.4 to 58.2)	60.7 (56.3 to 65.0)		
Week 40	51.9 (47.3 to 56.4)	56.2 (51.7 to 60.8)		
Week 44	53.0 (48.4 to 57.6)	60.9 (56.5 to 65.3)		
Week 48	56.2 (51.8 to 60.7)	60.6 (56.2 to 65.1)		
Week 52	54.3 (49.8 to 58.9)	60.4 (55.9 to 64.8)		
Week 56	51.9 (47.3 to 56.4)	58.7 (54.3 to 63.2)		
Week 60	56.0 (51.5 to 60.4)	58.7 (54.3 to 63.1)		
Week 64	56.5 (52.1 to 61.0)	57.9 (53.4 to 62.4)		
Week 68	56.0 (51.5 to 60.4)	57.9 (53.4 to 62.4)		
Week 72	56.2 (51.7 to 60.8)	58.5 (53.9 to 63.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants with ≤38 Letters in BCVA (20/200 or Worse Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants with ≤38 Letters in BCVA (20/200 or Worse Snellen Equivalent) in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (>38 and ≤38 letters) and region (U.S. and Canada, Asia, and rest of the world). All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	10.0 (7.3 to 12.8)	8.6 (6.1 to 11.1)		
Week 8	8.2 (5.5 to 10.8)	7.0 (4.6 to 9.4)		
Week 12	7.3 (4.9 to 9.8)	6.4 (4.0 to 8.8)		
Week 16	7.8 (5.3 to 10.4)	6.2 (3.8 to 8.5)		
Week 20	8.4 (5.7 to 11.0)	6.4 (4.0 to 8.8)		
Week 24	10.1 (7.1 to 13.0)	7.5 (4.9 to 10.1)		
Week 28	8.9 (6.1 to 11.7)	9.4 (6.6 to 12.3)		
Week 32	9.2 (6.4 to 12.0)	8.0 (5.4 to 10.7)		
Week 36	9.5 (6.6 to 12.4)	8.3 (5.7 to 11.0)		
Week 40	9.8 (6.8 to 12.7)	7.5 (4.9 to 10.1)		
Week 44	10.6 (7.5 to 13.6)	8.3 (5.6 to 11.0)		
Week 48	10.0 (7.1 to 13.0)	7.5 (4.9 to 10.1)		
Week 52	11.4 (8.3 to 14.5)	7.2 (4.7 to 9.8)		
Week 56	11.9 (8.8 to 15.1)	8.6 (5.8 to 11.4)		
Week 60	11.4 (8.3 to 14.5)	8.3 (5.7 to 11.0)		
Week 64	11.1 (8.0 to 14.2)	8.3 (5.6 to 11.0)		
Week 68	11.2 (8.0 to 14.3)	8.3 (5.6 to 11.0)		
Week 72	11.4 (8.3 to 14.6)	8.0 (5.4 to 10.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Change from Baseline in NEI VFQ-25 Questionnaire Composite Score at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Change from Baseline in NEI VFQ-25 Questionnaire Composite Score at Specified Timepoints Through Week 72

End point description:

The NEI VFQ-25 captures a patient’s perception of vision-related functioning and vision-related quality of life. The core measure includes 25 items that comprise 11 vision-related subscales and 1 item on

general health. The composite score ranges from 0 to 100, with higher scores indicating better vision-related functioning. For the MMRM analysis, the model adjusted for the treatment group, visit, visit-by-treatment group interaction, baseline NEI VFQ-25 Composite Score continuous), baseline BCVA score (≥55 and ≤54 letters), and region (U.S. and Canada, Asia, and the rest of the world). Observed NEI VFQ-25 assessments were used regardless of the occurrence of intercurrent events. Missing data were implicitly imputed. Invalid BCVA values were excluded. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 48, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: score on a scale				
arithmetic mean (confidence interval 95%)				
Week 24	7.0 (5.9 to 8.0)	8.2 (7.1 to 9.3)		
Week 48	7.0 (5.9 to 8.2)	8.3 (7.1 to 9.5)		
Week 72	7.8 (6.5 to 9.0)	8.5 (7.3 to 9.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Change from Baseline in Central Subfield Thickness in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Change from Baseline in Central Subfield Thickness in the Study Eye at Specified Timepoints Through Week 72

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. The Mixed Model of Repeated Measures (MMRM) analysis included the categorical covariates of treatment arm, visit, visit-by-treatment arm interaction, baseline CST (continuous), and randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)] as fixed effects. An unstructured covariance structure was used. Missing data were implicitly imputed by MMRM model assuming missing at random. Treatment policy strategy (i.e., all observed values used) was applied to all intercurrent events (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: microns				
arithmetic mean (confidence interval 95%)				
Week 4	-422.1 (-430.6 to -413.7)	-418.2 (-426.6 to -409.7)		
Week 8	-445.1 (-453.6 to -436.6)	-438.5 (-447.0 to -429.9)		
Week 12	-452.3 (-461.8 to -442.8)	-443.7 (-453.2 to -434.1)		
Week 16	-453.8 (-463.1 to -444.5)	-446.2 (-455.5 to -436.9)		
Week 20	-460.0 (-468.1 to -451.8)	-447.1 (-455.4 to -438.9)		
Week 24	-462.3 (-472.3 to -452.3)	-447.8 (-457.9 to -437.8)		
Week 28	-415.5 (-431.8 to -399.1)	-413.7 (-430.3 to -397.2)		
Week 32	-459.4 (-468.7 to -450.1)	-445.8 (-455.3 to -436.3)		
Week 36	-451.7 (-462.7 to -440.8)	-441.8 (-452.9 to -430.8)		
Week 40	-409.8 (-425.6 to -394.0)	-414.0 (-429.9 to -398.0)		
Week 44	-456.6 (-467.1 to -446.0)	-449.8 (-460.6 to -439.0)		
Week 48	-461.2 (-471.3 to -451.1)	-448.0 (-458.3 to -437.7)		
Week 52	-446.0 (-457.0 to -435.0)	-451.8 (-462.9 to -440.7)		
Week 56	-435.9 (-449.8 to -422.0)	-426.2 (-440.3 to -412.1)		
Week 60	-468.2 (-476.8 to -459.5)	-458.9 (-467.6 to -450.1)		
Week 64	-466.6 (-473.7 to -459.5)	-465.5 (-472.6 to -458.3)		
Week 68	-467.5 (-476.0 to -459.1)	-457.7 (-466.2 to -449.2)		
Week 72	-463.5 (-472.8 to -454.3)	-458.6 (-467.9 to -449.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants with Absence of Macular Edema in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants with Absence of Macular Edema in the Study Eye at Specified Timepoints Through Week 72

End point description:

Absence of diabetic macular edema was defined as achieving a central subfield thickness of <325 microns in the study eye. Central subfield thickness was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	83.8 (80.2 to 87.5)	82.4 (78.5 to 86.2)		
Week 8	92.6 (90.0 to 95.2)	91.2 (88.3 to 94.1)		
Week 12	93.4 (90.9 to 95.9)	91.5 (88.6 to 94.3)		
Week 16	94.5 (92.2 to 96.8)	92.8 (90.2 to 95.5)		
Week 20	94.5 (92.2 to 96.8)	93.1 (90.5 to 95.7)		
Week 24	93.7 (91.2 to 96.2)	91.7 (88.9 to 94.5)		
Week 28	82.5 (78.6 to 86.4)	84.0 (80.3 to 87.7)		
Week 32	93.2 (90.6 to 95.7)	90.3 (87.4 to 93.3)		
Week 36	91.8 (89.0 to 94.6)	89.5 (86.4 to 92.6)		
Week 40	80.0 (76.0 to 84.1)	80.7 (76.7 to 84.7)		
Week 44	93.2 (90.6 to 95.7)	90.9 (88.0 to 93.8)		
Week 48	92.6 (89.9 to 95.3)	89.8 (86.7 to 92.9)		
Week 52	88.5 (85.2 to 91.8)	90.9 (88.0 to 93.8)		
Week 56	87.4 (84.1 to 90.8)	84.3 (80.6 to 88.0)		
Week 60	93.7 (91.3 to 96.2)	92.8 (90.2 to 95.5)		
Week 64	94.3 (91.9 to 96.6)	93.4 (90.8 to 95.9)		
Week 68	93.2 (90.6 to 95.7)	91.4 (88.6 to 94.3)		

Week 72	92.4 (89.6 to 95.1)	91.2 (88.3 to 94.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye at Specified Timepoints Through Week 72

End point description:

Intraretinal fluid was measured in the study eye using optical coherence tomography (OCT) in the central subfield (center 1 mm) by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	45.5 (40.6 to 50.5)	40.6 (35.8 to 45.3)		
Week 8	63.1 (58.3 to 68.0)	61.7 (56.9 to 66.6)		
Week 12	53.2 (48.3 to 58.2)	51.0 (46.2 to 55.9)		
Week 16	55.4 (50.5 to 60.3)	51.9 (46.8 to 56.9)		
Week 20	59.0 (54.0 to 63.9)	56.5 (51.6 to 61.5)		
Week 24	77.0 (72.8 to 81.3)	70.8 (66.2 to 75.4)		
Week 28	53.8 (48.7 to 58.9)	51.5 (46.4 to 56.6)		
Week 32	67.7 (63.1 to 72.4)	67.2 (62.5 to 72.0)		
Week 36	62.8 (58.1 to 67.5)	57.6 (52.6 to 62.6)		

Week 40	52.7 (47.7 to 57.7)	51.0 (46.0 to 56.1)		
Week 44	66.4 (61.6 to 71.2)	63.4 (58.5 to 68.3)		
Week 48	74.3 (69.9 to 78.8)	69.7 (65.0 to 74.3)		
Week 52	66.9 (62.2 to 71.6)	63.4 (58.5 to 68.2)		
Week 56	60.9 (56.0 to 65.9)	58.7 (53.7 to 63.6)		
Week 60	71.6 (67.0 to 76.1)	72.7 (68.2 to 77.2)		
Week 64	76.5 (72.2 to 80.8)	72.7 (68.2 to 77.2)		
Week 68	74.6 (70.2 to 79.0)	71.3 (66.8 to 75.9)		
Week 72	78.1 (73.9 to 82.3)	74.4 (69.9 to 78.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants with Absence of Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants with Absence of Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 72

End point description:

Subretinal fluid was measured in the study eye using optical coherence tomography (OCT) in the central subfield (center 1 mm) by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	66.1 (61.4 to 70.8)	65.0 (60.3 to 69.7)		
Week 8	89.6 (86.5 to 92.6)	90.1 (87.0 to 93.1)		

Week 12	94.0 (91.6 to 96.4)	93.9 (91.5 to 96.4)		
Week 16	95.3 (93.2 to 97.5)	95.6 (93.5 to 97.7)		
Week 20	95.9 (93.9 to 97.9)	94.5 (92.2 to 96.8)		
Week 24	96.2 (94.2 to 98.1)	93.4 (90.8 to 95.9)		
Week 28	89.3 (86.2 to 92.5)	90.1 (87.0 to 93.1)		
Week 32	95.6 (93.6 to 97.7)	94.5 (92.2 to 96.8)		
Week 36	95.1 (92.9 to 97.3)	92.3 (89.6 to 95.0)		
Week 40	89.6 (86.5 to 92.7)	89.3 (86.1 to 92.4)		
Week 44	95.4 (93.2 to 97.5)	92.8 (90.2 to 95.5)		
Week 48	93.4 (90.9 to 95.9)	89.5 (86.4 to 92.6)		
Week 52	92.6 (89.9 to 95.3)	93.6 (91.2 to 96.1)		
Week 56	93.4 (90.9 to 95.9)	90.1 (87.1 to 93.1)		
Week 60	97.0 (95.3 to 98.7)	94.8 (92.5 to 97.0)		
Week 64	96.7 (94.9 to 98.5)	95.9 (93.8 to 97.9)		
Week 68	97.6 (96.0 to 99.1)	93.9 (91.6 to 96.3)		
Week 72	95.4 (93.2 to 97.5)	93.1 (90.6 to 95.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1 and 2: Percentage of Participants with Absence of Intraretinal Fluid and Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 72

End point title	Parts 1 and 2: Percentage of Participants with Absence of Intraretinal Fluid and Subretinal Fluid in the Study Eye at Specified Timepoints Through Week 72

End point description:

Intraretinal fluid and subretinal fluid were measured in the study eye using optical coherence tomography (OCT) in the central subfield (center 1 mm) by a central reading center. The weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 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, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	33.0 (28.3 to 37.6)	29.3 (24.9 to 33.7)		
Week 8	59.3 (54.4 to 64.1)	59.3 (54.3 to 64.2)		
Week 12	52.7 (47.7 to 57.6)	50.2 (45.3 to 55.1)		
Week 16	54.9 (49.9 to 59.8)	51.3 (46.3 to 56.3)		
Week 20	58.2 (53.2 to 63.1)	55.4 (50.5 to 60.4)		
Week 24	76.0 (71.6 to 80.3)	68.6 (63.8 to 73.4)		
Week 28	52.7 (47.6 to 57.8)	51.2 (46.1 to 56.3)		
Week 32	67.2 (62.6 to 71.8)	66.4 (61.6 to 71.2)		
Week 36	62.8 (58.1 to 67.5)	56.5 (51.5 to 61.5)		
Week 40	52.7 (47.7 to 57.7)	50.2 (45.1 to 55.2)		
Week 44	64.7 (59.9 to 69.6)	60.9 (56.0 to 65.8)		
Week 48	70.8 (66.1 to 75.4)	65.8 (61.0 to 70.6)		
Week 52	65.8 (61.1 to 70.6)	61.7 (56.8 to 66.6)		
Week 56	60.7 (55.7 to 65.6)	58.1 (53.2 to 63.0)		
Week 60	71.0 (66.4 to 75.6)	71.6 (67.0 to 76.2)		
Week 64	75.4 (71.1 to 79.8)	71.9 (67.3 to 76.4)		
Week 68	74.3 (69.9 to 78.8)	70.8 (66.2 to 75.3)		
Week 72	77.0 (72.8 to 81.3)	71.6 (67.0 to 76.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Change from Week 24 in BCVA in the Study Eye at Specified Timepoints Through Week 72

End point title	Part 2: Change from Week 24 in BCVA in the Study Eye at

	Specified Timepoints Through Week 72

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 included the categorical covariates of treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), and randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)] as fixed effects. An unstructured covariance structure was used. Missing data were implicitly imputed by MMRM model assuming missing at random. Treatment policy strategy (i.e., all observed values used) was applied to all intercurrent events (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Weeks 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, and 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	340	331		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 28	-0.8 (-1.6 to 0.0)	-1.2 (-2.0 to -0.4)		
Week 32	0.2 (-0.6 to 0.9)	0.2 (-0.6 to 1.0)		
Week 36	-0.1 (-0.8 to 0.7)	0.1 (-0.7 to 0.9)		
Week 40	-1.3 (-2.4 to -0.2)	-1.4 (-2.4 to -0.3)		
Week 44	-0.6 (-1.6 to 0.4)	0.0 (-1.0 to 1.0)		
Week 48	-0.1 (-1.1 to 0.9)	0.2 (-0.8 to 1.1)		
Week 52	-0.6 (-1.6 to 0.4)	0.3 (-0.6 to 1.3)		
Week 56	-1.1 (-2.1 to 0.0)	-0.6 (-1.7 to 0.5)		
Week 60	0.0 (-1.1 to 1.0)	-0.1 (-1.2 to 0.9)		
Week 64	-0.2 (-1.3 to 0.8)	-0.2 (-1.3 to 0.9)		
Week 68	-0.1 (-1.2 to 1.0)	-0.5 (-1.6 to 0.6)		
Week 72	-0.2 (-1.3 to 1.0)	-0.3 (-1.5 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

End point title	Part 2: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Weeks 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, and 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	86.3 (82.9 to 89.8)	83.8 (80.0 to 87.5)		
Week 32	88.8 (85.6 to 92.0)	87.9 (84.6 to 91.2)		
Week 36	89.3 (86.2 to 92.5)	87.9 (84.6 to 91.2)		
Week 40	87.4 (84.0 to 90.8)	86.0 (82.4 to 89.5)		
Week 44	87.4 (84.0 to 90.8)	88.4 (85.2 to 91.7)		
Week 48	88.5 (85.3 to 91.7)	87.3 (83.9 to 90.7)		
Week 52	86.3 (82.8 to 89.8)	87.6 (84.2 to 91.0)		
Week 56	85.7 (82.2 to 89.3)	85.4 (81.8 to 89.0)		
Week 60	87.7 (84.3 to 91.0)	86.2 (82.7 to 89.8)		
Week 64	86.3 (82.8 to 89.8)	85.9 (82.4 to 89.5)		
Week 68	87.1 (83.7 to 90.5)	85.4 (81.8 to 89.0)		
Week 72	86.6 (83.1 to 90.0)	84.0 (80.3 to 87.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

End point title	Part 2: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Weeks 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, and 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	82.8 (79.0 to 86.6)	81.3 (77.3 to 85.2)		
Week 32	87.1 (83.7 to 90.6)	86.0 (82.4 to 89.5)		
Week 36	84.7 (81.0 to 88.4)	85.4 (81.8 to 89.0)		
Week 40	82.8 (78.9 to 86.6)	81.6 (77.6 to 85.5)		
Week 44	84.1 (80.4 to 87.9)	86.8 (83.4 to 90.2)		
Week 48	84.4 (80.7 to 88.1)	84.8 (81.2 to 88.5)		
Week 52	82.8 (78.9 to 86.6)	85.4 (81.8 to 89.0)		
Week 56	80.0 (76.0 to 84.1)	81.8 (77.9 to 85.8)		
Week 60	83.6 (79.8 to 87.4)	82.6 (78.8 to 86.5)		
Week 64	81.7 (77.7 to 85.6)	83.2 (79.4 to 87.0)		
Week 68	82.2 (78.3 to 86.1)	80.7 (76.7 to 84.7)		
Week 72	82.5 (78.6 to 86.3)	80.7 (76.7 to 84.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

End point title	Part 2: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Weeks 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, and 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	72.7 (68.2 to 77.2)	69.7 (65.0 to 74.4)		
Week 32	78.4 (74.2 to 82.6)	75.5 (71.1 to 79.9)		
Week 36	74.1 (69.6 to 78.5)	80.2 (76.1 to 84.2)		
Week 40	71.0 (66.4 to 75.6)	71.6 (67.0 to 76.2)		
Week 44	73.7 (69.3 to 78.2)	73.0 (68.5 to 77.6)		
Week 48	76.5 (72.2 to 80.8)	74.1 (69.6 to 78.6)		
Week 52	71.3 (66.7 to 75.9)	74.1 (69.6 to 78.6)		
Week 56	69.4 (64.7 to 74.1)	68.3 (63.6 to 73.1)		

Week 60	74.3 (69.8 to 78.7)	71.6 (67.0 to 76.2)		
Week 64	74.6 (70.1 to 79.0)	71.6 (67.0 to 76.2)		
Week 68	73.2 (68.7 to 77.7)	69.2 (64.5 to 73.8)		
Week 72	72.9 (68.4 to 77.5)	70.3 (65.6 to 74.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants Avoiding a Loss of >0 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

End point title	Part 2: Percentage of Participants Avoiding a Loss of >0 Letters in BCVA from Week 24 in the Study Eye at Specified Timepoints Through Week 72

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 weighted percentage of participants was estimated based on the Cochran-Mantel Haenszel (CMH) weights stratified by randomization stratification factors [baseline BCVA (≤34, 35-54, and ≥55 letters), and region (U.S. and Canada, Asia, and rest of the world)]. All observed values were used regardless of the occurrence of an intercurrent event (discontinuation of treatment due to AEs or lack of efficacy, use of prohibited therapy). Missing assessments were imputed by last observation carried forward. 95% CI is a rounding of 95.03% CI.

End point type	Secondary

End point timeframe:

Weeks 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, and 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	363		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	48.9 (43.8 to 54.0)	45.4 (40.4 to 50.5)		
Week 32	56.0 (50.9 to 61.1)	52.9 (47.8 to 58.0)		
Week 36	55.5 (50.4 to 60.5)	55.1 (50.0 to 60.2)		
Week 40	53.0 (47.9 to 58.0)	48.2 (43.1 to 53.3)		
Week 44	53.0 (47.9 to 58.0)	54.0 (49.0 to 59.1)		
Week 48	56.5 (51.5 to 61.6)	53.5 (48.4 to 58.6)		

Week 52	56.0 (50.9 to 61.1)	56.5 (51.4 to 61.5)		
Week 56	54.9 (49.8 to 60.0)	53.2 (48.1 to 58.2)		
Week 60	55.9 (50.9 to 61.0)	51.0 (45.9 to 56.1)		
Week 64	54.6 (49.5 to 59.7)	52.1 (47.0 to 57.2)		
Week 68	55.4 (50.4 to 60.4)	52.3 (47.3 to 57.4)		
Week 72	55.4 (50.4 to 60.5)	52.7 (47.6 to 57.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Percentage of Participants on Different Treatment Intervals at Week 68

End point title	Part 2: Percentage of Participants on Different Treatment Intervals at Week 68

End point description:

In Part 2 of the study, participants in both the faricimab Q4W and aflibercept Q4W arms in Part 1 received 6 mg faricimab intravitreal injections administered according to a personalized treatment interval (PTI) dosing regimen in intervals between Q4W and Q16W. At faricimab dosing visits, treatment intervals were maintained or adjusted (i.e., increased by 4 weeks or decreased by 4, 8, or 12 weeks), based on central subfield thickness (CST) and BCVA values.

End point type	Secondary

End point timeframe:

Week 68

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	330	315		
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 4 Weeks (Q4W)	34.5 (29.4 to 39.7)	32.4 (27.2 to 37.6)		
Once Every 8 Weeks (Q8W)	20.0 (15.7 to 24.3)	17.5 (13.3 to 21.7)		
Once Every 12 Weeks (Q12W)	8.5 (5.5 to 11.5)	11.1 (7.6 to 14.6)		
Once Every 16 Weeks (Q16W)	37.0 (31.8 to 42.2)	39.0 (33.7 to 44.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and Severity of Ocular Adverse Events in the Study Eye, with Severity Determined According to Adverse Event Severity Grading Scale

End point title	Incidence and Severity of Ocular Adverse Events in the Study Eye, with Severity Determined According to Adverse Event Severity Grading Scale

End point description:

This analysis of adverse events (AEs) only includes ocular AEs that occurred in the study eye. 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:

Part 1: From first dose up to Week 24; Part 2: from Week 24 through Week 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	359	342	365	361
Units: Participants				
Adverse Event (AE)	130	118	89	98
AE by Severity: Mild	63	69	65	65
AE by Severity: Moderate	52	43	18	27
AE by Severity: Severe	15	6	6	6
Serious Adverse Event (SAE)	26	12	9	13
AE Leading to Withdrawal from Study Treatment	5	3	3	2
Treatment Related AEs	14	11	15	6
Treatment Related SAEs	4	0	3	2
Any AE of Special Interest (AESI)	21	9	8	12
AESI: Drop in Visual Acuity Score ≥30	15	7	6	6
AESI: Associated with Severe IOI	0	1	0	0
AESI: Interv. Req. to Prevent Perm. Vision Loss	6	1	2	6

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Number of Study Drug Injections Received in the Study Eye from Week 24 Through Week 72

End point title	Part 2: Number of Study Drug Injections Received in the Study

	Eye from Week 24 Through Week 72

End point description:

End point type	Secondary

End point timeframe:

From Week 24 to Week 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	359	342		
Units: Injections				
median (full range (min-max))	5.0 (1 to 12)	4.0 (1 to 12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Ocular Adverse Events in the Fellow Eye

End point title	Incidence of Ocular Adverse Events in the Fellow Eye

End point description:

This analysis of adverse events (AEs) only includes ocular AEs that occurred in the fellow eye. 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:

Part 1: From first dose up to Week 24; Part 2: from Week 24 through Week 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	359	342	365	361
Units: Participants				
Adverse Event (AE)	70	51	31	33
Serious Adverse Event (SAE)	1	0	1	1
Any AE of Special Interest (AESI)	1	0	1	1
AESI: Drop in Visual Acuity Score ≥30	1	0	1	1

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Non-Ocular Adverse Events

End point title	Incidence of Non-Ocular Adverse Events

End point description:

This analysis of adverse events (AEs) only includes non-ocular (systemic) AEs. Investigators sought information on adverse events (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:

Part 1: From first dose up to Week 24; Part 2: from Week 24 through Week 72

End point values	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W (Part 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	359	342	365	361
Units: Participants				
Adverse Event (AE)	191	174	123	134
Serious Adverse Event (SAE)	30	41	22	23
AE Leading to Withdrawal from Study Treatment	3	3	0	1
Any AE of Special Interest (AESI)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Drug Antibodies (ADAs) to Faricimab at Baseline and Post-Baseline During the Study

End point title	Number of Participants with Anti-Drug Antibodies (ADAs) to Faricimab at Baseline and Post-Baseline During the Study

End point description:

Anti-drug antibodies (ADAs) against fariciamb were detected in plasma using a validated bridging enzyme-linked immunosorbent assay (ELISA). The number 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. Treatment-unaffected ADA-positive is a post-baseline sample with a titer that is lower than 4-fold the ADA-positive baseline titer (faricimab arm) or the ADA-positive titer prior to first faricimab injection (aflibercept arm).

End point type	Secondary

End point timeframe:

Predose at Day 1 (Baseline), Weeks 4, 24, 28, 52, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)	All Faricimab Participants	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	366	342	708	
Units: Participants				
Baseline (BL): Total ADA-Positive	4	5	9	
Post-BL: Total ADA-Positive	62	27	89	
Post-BL: Treatment-Emergent ADA-Positive	60	23	83	
Post-BL: Treatment-Unaffected ADA-Positive	2	4	6	

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

End point description:

End point type	Secondary

End point timeframe:

Predose at Day 1 (Baseline), Weeks 4, 24, 28, 52, and 72

End point values	Arm A: Faricimab Q4W (Part 1), Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W (Part 1), Faricimab PTI (Part 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	365	342		
Units: microgram per millilitre (µg/mL)				
arithmetic mean (standard deviation)				
Baseline (n = 359, 0)	0.0001 (± 0.0009)	999999 (± 999999)		
Week 4 (n = 345, 0)	0.0222 (± 0.0176)	999999 (± 999999)		

Week 24 (n = 321, 324)	0.0257 (± 0.0217)	0.0005 (± 0.0014)		
Week 28 (n = 323, 314)	0.0055 (± 0.0086)	0.0026 (± 0.0084)		
Week 52 (n = 318, 300)	0.0089 (± 0.0142)	0.0090 (± 0.0136)		
Week 72 (n = 279, 272)	0.0087 (± 0.0140)	0.0099 (± 0.0167)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part 1: From first dose up to Week 24; Part 2: from Week 24 through Week 72

Adverse event reporting additional description:

Safety analysis population: all subjects who received ≥1 study drug injection (faricimab or aflibercept). For Part 2, this included: in Arm A, those with Week 24 treatment or dose hold, or if none, follow-up beyond Day 168; in Arm B, those who received ≥1 faricimab dose. The eye type (study/fellow) in which an ocular AE had occurred is specified.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Arm A: Faricimab Q4W (Part 1)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A will receive faricimab 6 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Reporting group title	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)

Reporting group description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was to be administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Reporting group title	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)

Reporting group description:

In Part 2 (from Week 24 to Week 72), participants received faricimab 6 mg by IVT injection according to a personalized treatment interval (PTI) dosing regimen. To preserve masking for Part 2, a sham procedure was administered during study visits at which no faricimab treatment was administered (according to the PTI dosing regimen).

Reporting group title	Arm B: Aflibercept Q4W (Part 1)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm B will receive aflibercept 2 milligrams (mg) by IVT injection once every 4 weeks (Q4W) from Day 1 through Week 20 (a total of 6 injections).

Serious adverse events	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 365 (8.77%)	51 / 342 (14.91%)	55 / 359 (15.32%)
number of deaths (all causes)	1	1	4
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer			

subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder adenocarcinoma stage unspecified			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			

subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Aortic aneurysm			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Secondary hypertension			

subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery aneurysm			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal transplant			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament operation			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Stent-graft endoleak			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 365 (0.00%)	2 / 342 (0.58%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	2 / 359 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2

Chest pain			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystocele			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 365 (0.27%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pickwickian syndrome			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 365 (0.27%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Intraocular pressure increased	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Eye injury	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 365 (0.27%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Shunt occlusion			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 365 (0.00%)	2 / 342 (0.58%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt stenosis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 365 (0.27%)	2 / 342 (0.58%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	3 / 359 (0.84%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	2 / 359 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			

subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 365 (0.00%)	2 / 342 (0.58%)	2 / 359 (0.56%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 365 (0.55%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 365 (0.00%)	2 / 342 (0.58%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deficiency anaemia			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric lymphadenitis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cystoid macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 365 (0.55%)	1 / 342 (0.29%)	5 / 359 (1.39%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular ischaemia	Additional description: AEs occurred in the study eye		

subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-infectious endophthalmitis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal tear	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal artery occlusion	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 365 (0.55%)	2 / 342 (0.58%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal ischaemia	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal artery embolism	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhegmatogenous retinal detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 365 (0.55%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced	Additional description: AEs occurred in the study eye		

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiretinal membrane	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iridocyclitis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iris neovascularisation	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular hole	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior capsule opacification	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment	Additional description: AEs occurred in the study eye		

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal neovascularisation	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitritis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract	Additional description: AEs occurred in the fellow eye (Arm A, Part 1) and the study eye (Arm B, Part 2).		
subjects affected / exposed	1 / 365 (0.27%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular oedema	Additional description: All AEs occurred in the study eye, except for 1 subject had 1 event in the fellow eye (Arm A, Part 2).		
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	5 / 359 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal vein occlusion	Additional description: All AEs occurred in the study eye, except for 1 subject had 1 event in the fellow eye (Arm B, Part 1).		
subjects affected / exposed	2 / 365 (0.55%)	3 / 342 (0.88%)	5 / 359 (1.39%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal bulb deformity			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	2 / 365 (0.55%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder disorder			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic steatosis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis interstitial			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			

subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic nephropathy			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteonecrosis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint effusion			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility decreased			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polymyositis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 365 (0.82%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis acute			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 365 (0.55%)	2 / 342 (0.58%)	3 / 359 (0.84%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Endophthalmitis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 365 (0.27%)	2 / 342 (0.58%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			

subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth infection			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract candidiasis			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 365 (0.27%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 365 (0.00%)	0 / 342 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypervolaemia			

subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 365 (0.00%)	1 / 342 (0.29%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm B: Aflibercept Q4W (Part 1)		
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 361 (9.42%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder adenocarcinoma stage unspecified			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm of thyroid gland			

subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thyroid cancer				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Papillary thyroid cancer				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypertensive crisis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic dissection				

subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic aneurysm				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Secondary hypertension				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral artery aneurysm				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Knee operation				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal transplant				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament operation				

subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Stent-graft endoleak			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystocele			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pickwickian syndrome				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary hypertension				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive sleep apnoea syndrome				

subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Intraocular pressure increased	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Eye injury	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shunt occlusion			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Fracture				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shunt stenosis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				

subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	3 / 361 (0.83%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 2			
Cardiac failure congestive				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic valve incompetence				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stress cardiomyopathy				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Altered state of consciousness				

subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral sensorimotor neuropathy				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoaesthesia				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				

subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deficiency anaemia			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric lymphadenitis			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cystoid macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 361 (0.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Macular ischaemia	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-infectious endophthalmitis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal tear	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 361 (0.55%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Retinal artery occlusion	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal ischaemia	Additional description: AEs occurred in the study eye		

subjects affected / exposed	2 / 361 (0.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Retinal artery embolism	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhegmatogenous retinal detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uveitis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Visual acuity reduced	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vitreous haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epiretinal membrane	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glaucoma	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iridocyclitis	Additional description: AEs occurred in the study eye		

subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iris neovascularisation	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Macular hole	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Posterior capsule opacification	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal neovascularisation	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vitritis	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cataract	Additional description: AEs occurred in the fellow eye (Arm A, Part 1) and the study eye (Arm B, Part 2).		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Macular oedema	Additional description: All AEs occurred in the study eye, except for 1 subject had 1 event in the fellow eye (Arm A, Part 2).		

subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retinal vein occlusion	Additional description: All AEs occurred in the study eye, except for 1 subject had 1 event in the fellow eye (Arm B, Part 1).			
subjects affected / exposed	3 / 361 (0.83%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Duodenal bulb deformity				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive pancreatitis				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peptic ulcer				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Duodenitis				

subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large intestine polyp				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal inflammation				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile duct stone				

subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gallbladder disorder				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic steatosis				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Diabetic foot				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Calculus urinary				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				

subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urethral stenosis				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis interstitial				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
End stage renal disease				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic nephropathy				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephropathy				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				

subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint effusion			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mobility decreased			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Polymyositis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
COVID-19				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis acute				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endophthalmitis	Additional description: AEs occurred in the study eye			
subjects affected / exposed	1 / 361 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Kidney infection				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				

subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Necrotising fasciitis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tooth infection				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract candidiasis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 361 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypervolaemia			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Arm A: Faricimab Q4W (Part 1)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 365 (18.36%)	118 / 342 (34.50%)	109 / 359 (30.36%)
Investigations			
Intraocular pressure increased	Additional description: AEs occurred in the study eye		

subjects affected / exposed	9 / 365 (2.47%)	15 / 342 (4.39%)	16 / 359 (4.46%)
occurrences (all)	11	34	21
Vascular disorders			
Hypertension			
subjects affected / exposed	15 / 365 (4.11%)	8 / 342 (2.34%)	12 / 359 (3.34%)
occurrences (all)	15	8	13
Eye disorders			
Conjunctival haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	10 / 365 (2.74%)	7 / 342 (2.05%)	10 / 359 (2.79%)
occurrences (all)	11	8	11
Vitreous detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	11 / 365 (3.01%)	14 / 342 (4.09%)	6 / 359 (1.67%)
occurrences (all)	11	14	6
Epiretinal membrane	Additional description: AEs occurred in the study eye		
subjects affected / exposed	3 / 365 (0.82%)	11 / 342 (3.22%)	3 / 359 (0.84%)
occurrences (all)	3	11	3
Macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 365 (0.55%)	14 / 342 (4.09%)	7 / 359 (1.95%)
occurrences (all)	2	16	12
Cystoid macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 365 (0.27%)	10 / 342 (2.92%)	11 / 359 (3.06%)
occurrences (all)	1	10	15
Cataract	Additional description: AEs occurred in the study eye		
subjects affected / exposed	3 / 365 (0.82%)	14 / 342 (4.09%)	14 / 359 (3.90%)
occurrences (all)	3	14	14
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 365 (3.84%)	46 / 342 (13.45%)	42 / 359 (11.70%)
occurrences (all)	14	46	42
Nasopharyngitis			
subjects affected / exposed	5 / 365 (1.37%)	16 / 342 (4.68%)	10 / 359 (2.79%)
occurrences (all)	5	16	10

Non-serious adverse events	Arm B: Aflibercept Q4W (Part 1)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 361 (18.28%)		

Investigations			
Intraocular pressure increased	Additional description: AEs occurred in the study eye		
subjects affected / exposed	12 / 361 (3.32%)		
occurrences (all)	22		
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 361 (2.77%)		
occurrences (all)	10		
Eye disorders			
Conjunctival haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	14 / 361 (3.88%)		
occurrences (all)	14		
Vitreous detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	9 / 361 (2.49%)		
occurrences (all)	9		
Epiretinal membrane	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 361 (0.55%)		
occurrences (all)	2		
Macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 361 (0.00%)		
occurrences (all)	0		
Cystoid macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	3 / 361 (0.83%)		
occurrences (all)	3		
Cataract	Additional description: AEs occurred in the study eye		
subjects affected / exposed	7 / 361 (1.94%)		
occurrences (all)	7		
Infections and infestations			
COVID-19			
subjects affected / exposed	12 / 361 (3.32%)		
occurrences (all)	12		
Nasopharyngitis			
subjects affected / exposed	7 / 361 (1.94%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 November 2020	Protocol Version 2, the summary of major changes from Version 1 were as follows: -Due to extenuating circumstances, such as the Coronavirus Disease 2019 (COVID-19) pandemic, patients may not have had the ability to complete certain trial activities, therefore, in order to ensure adequate power for the primary endpoint, the sample size was increased to mitigate the loss of patients, loss of data, and the potential impact of protocol deviations affecting efficacy analyses.; -Clarified that missed mandatory pharmacokinetic (PK), pharmacodynamic (PD), or anti-drug antibody (ADA) samples be obtained at the next scheduled visit the patient attended.; -Clarified administration guidelines of the National Eye Institute 25-Item Visual Functioning Questionnaire (NEI VFQ-25) to include interviews over the telephone.; -Corrected the description of the BCVA stratification factor's text in the protocol (programming in IxRS was initially correct so no changes in programming were necessary).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported