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 Branch Retinal Vein Occlusion

Summary

EudraCT number	2020-000440-63
Trial protocol	HU DE PT AT CZ PL IT
Global end of trial date	12 June 2023

Results information

Result version number	v1
This version publication date	26 June 2024
First version publication date	26 June 2024

Trial information

Trial identification

Sponsor protocol code	GR41984

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04740905
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 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 June 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: 68
Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Brazil: 8
Country: Number of subjects enrolled	China: 63
Country: Number of subjects enrolled	Czechia: 18
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hong Kong: 8
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Japan: 34
Country: Number of subjects enrolled	Korea, Republic of: 48
Country: Number of subjects enrolled	Poland: 47
Country: Number of subjects enrolled	Portugal: 9
Country: Number of subjects enrolled	Russian Federation: 17
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Spain: 14

Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	United States: 126
Worldwide total number of subjects	553
EEA total number of subjects	125

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)	277
From 65 to 84 years	262
85 years and over	14

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 768 patients were screened; 9 of these patients were rescreened and randomized in the study. A total of 215 patients failed screening due to not meeting the inclusion criteria. A total of 553 patients with BRVO were randomized 1:1 into the study: 276 to the faricimab Q4W arm and 277 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 were randomly assigned to Arm A to 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 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).

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 were randomly assigned to Arm B to 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 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).

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	276	277
Received ≥1 Dose of Study Drug (Part 1)	276	274
Completed Part 1	272	274
Started Part 2	272	274
Completed	245	244
Not completed	31	33
Adverse event, serious fatal	2	2
Consent withdrawn by subject	14	12
Physician decision	-	4
Adverse event, non-fatal	1	4
Did Not Return to Hospital Due to COVID19 Epidemic	1	-
Non-Compliance With Study Drug	2	1
Lost to follow-up	9	6
Patient Refused to Continue Study	1	-
Patient Missed Week 72 Visit Due to SAE	1	1
Protocol deviation	-	3

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 were randomly assigned to Arm A to 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 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), Faricimab PTI (Part 2)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants were randomly assigned to Arm B to 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 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 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	276	277	553
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)	133	144	277
From 65-84 years	133	129	262
85 years and over	10	4	14
Age Continuous Units: Years			
arithmetic mean	64.3	63.8	
standard deviation	± 10.7	± 10.6	-
Sex: Female, Male Units: Participants			
Female	133	147	280
Male	143	130	273
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	0	3
Asian	90	94	184
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	6	7	13
White	172	172	344

More than one race	0	0	0
Unknown or Not Reported	4	4	8
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	47	51	98
Not Hispanic or Latino	224	224	448
Unknown or Not Reported	5	2	7
Region of Enrollment Units: Subjects			
Rest of the World	129	128	257
Asia	85	85	170
USA and Canada	62	64	126
Number of Participants by the Eye (Left or Right) Chosen as the Study Eye Units: Subjects			
Left Eye	140	127	267
Right Eye	136	150	286
Number of Participants by the BCVA Letter Score Categories in the Study Eye Units: Subjects			
≤54 Letters (20/80 or Worse)	89	90	179
≥55 Letters (20/80 or Better)	187	187	374
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye Units: ETDRS Letters			
arithmetic mean	57.50	57.64	
standard deviation	± 13.04	± 12.15	-

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 were to receive faricimab 6 milligrams (mg) administered by intravitreal (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 were to receive aflibercept 2 milligrams (mg) administered by intravitreal (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 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 were to receive aflibercept 2 milligrams (mg) administered by intravitreal (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	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	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	276	277	276
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	17.5	
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 the World			
Asia			
USA and Canada			
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			
≤54 Letters (20/80 or Worse)			
≥55 Letters (20/80 or Better)			
Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye			
Units: ETDRS Letters			
arithmetic mean	16.9	17.5	
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	277	248	244

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 the World Asia USA and Canada			
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			
≤54 Letters (20/80 or Worse) ≥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 B: Aflibercept Q4W (Part 1)	Arm A: Faricimab Q4W to Faricimab PTI (Part 2)	Arm B: Aflibercept Q4W to Faricimab PTI (Part 2)
Number of subjects	274	270	267
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 the World Asia USA and Canada			
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			
≤54 Letters (20/80 or Worse) ≥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	All Faricimab Participants		
Number of subjects	540		
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 the World Asia USA and Canada			
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			
≤54 Letters (20/80 or Worse) ≥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

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 were randomly assigned to Arm A to 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 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), Faricimab PTI (Part 2)

Reporting group description:

In Part 1 (Day 1 through Week 24), participants were randomly assigned to Arm B to 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 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	Intention-to-treat

Subject analysis set description:

In Part 1 (Day 1 through Week 24), participants randomly assigned to Arm A were to receive faricimab 6 milligrams (mg) administered by intravitreal (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 were to receive aflibercept 2 milligrams (mg) administered by intravitreal (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 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 were to receive aflibercept 2 milligrams (mg) administered by intravitreal (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	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	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 (≥55 and ≤54 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	276	277		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)	16.9 (15.7 to 18.1)	17.5 (16.3 to 18.6)		

Statistical analyses

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	553
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.84

Notes:

[1] - 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.

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.

Comparison groups	Arm A: Faricimab Q4W (Part 1) v Arm B: Aflibercept Q4W (Part 1)
Number of subjects included in analysis	553
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4978 [2]
Method	Mixed Model of Repeated Measures
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.84

Notes:

[2] - Tested at a two-sided 0.0497 significance level.

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 (≥55 and ≤54 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	276	277		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 4	11.5 (10.5 to 12.5)	12.4 (11.4 to 13.4)		
Week 8	13.7 (12.6 to 14.7)	15.1 (14.1 to 16.2)		
Week 12	15.1 (14.0 to 16.2)	15.9 (14.8 to 17.0)		
Week 16	15.5 (14.4 to 16.6)	16.5 (15.4 to 17.7)		
Week 20	16.3 (15.2 to 17.4)	17.3 (16.1 to 18.4)		
Week 24	16.9 (15.7 to 18.1)	17.5 (16.3 to 18.6)		

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 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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	34.3 (28.9 to 39.8)	36.9 (31.5 to 42.3)		
Week 8	41.2 (35.6 to 46.9)	46.7 (41.0 to 52.3)		
Week 12	51.0 (45.3 to 56.7)	52.1 (46.3 to 57.8)		
Week 16	53.6 (47.8 to 59.3)	56.4 (50.8 to 62.1)		
Week 20	56.1 (50.3 to 61.8)	58.9 (53.3 to 64.6)		
Week 24	56.1 (50.4 to 61.9)	60.4 (54.7 to 66.0)		

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 (≥55 and ≤54 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 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)	56.1 (50.4 to 61.9)	60.4 (54.7 to 66.0)		

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	553
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	3.8

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	57.5 (51.8 to 63.3)	59.2 (53.6 to 64.9)		
Week 8	69.1 (63.8 to 74.5)	69.0 (63.6 to 74.4)		
Week 12	75.0 (69.9 to 80.1)	74.8 (69.7 to 79.8)		
Week 16	72.1 (66.9 to 77.3)	76.6 (71.6 to 81.5)		
Week 20	75.3 (70.3 to 80.4)	79.1 (74.3 to 83.9)		
Week 24	77.5 (72.6 to 82.4)	77.3 (72.4 to 82.2)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	75.7 (70.7 to 80.7)	79.1 (74.4 to 83.9)		
Week 8	84.0 (79.7 to 88.3)	88.1 (84.3 to 91.9)		
Week 12	87.0 (83.1 to 90.9)	87.0 (83.1 to 91.0)		
Week 16	85.9 (81.8 to 89.9)	88.8 (85.1 to 92.5)		
Week 20	88.4 (84.6 to 92.2)	90.3 (86.8 to 93.7)		
Week 24	90.9 (87.6 to 94.3)	89.6 (86.0 to 93.1)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	90.2 (86.8 to 93.6)	93.2 (90.3 to 96.1)		

Week 8	92.7 (89.7 to 95.8)	96.8 (94.7 to 98.8)		
Week 12	94.9 (92.4 to 97.5)	94.2 (91.5 to 97.0)		
Week 16	93.8 (91.1 to 96.6)	94.9 (92.4 to 97.5)		
Week 20	94.9 (92.4 to 97.5)	96.0 (93.8 to 98.3)		
Week 24	96.4 (94.2 to 98.6)	95.3 (92.9 to 97.8)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	99.3 (98.3 to 100.0)	98.9 (97.7 to 100.0)		
Week 8	99.3 (98.3 to 100.0)	98.9 (97.7 to 100.0)		
Week 12	99.3 (98.3 to 100.0)	98.9 (97.7 to 100.0)		
Week 16	99.3 (98.3 to 100.0)	98.6 (97.2 to 99.9)		
Week 20	99.6 (98.9 to 100.0)	98.6 (97.2 to 99.9)		
Week 24	99.6 (98.9 to 100.0)	98.6 (97.2 to 99.9)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	98.5 (97.1 to 99.9)	98.9 (97.7 to 100.0)		
Week 8	98.5 (97.1 to 100.0)	98.9 (97.7 to 100.0)		
Week 12	98.5 (97.1 to 99.9)	98.9 (97.7 to 100.0)		
Week 16	98.5 (97.1 to 99.9)	98.2 (96.7 to 99.7)		
Week 20	99.3 (98.3 to 100.0)	98.6 (97.2 to 99.9)		
Week 24	99.6 (98.9 to 100.0)	98.2 (96.7 to 99.7)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	97.1 (95.1 to 99.1)	98.6 (97.2 to 99.9)		
Week 8	97.8 (96.1 to 99.5)	98.6 (97.2 to 99.9)		
Week 12	97.8 (96.1 to 99.5)	98.9 (97.7 to 100.0)		
Week 16	97.8 (96.1 to 99.5)	98.2 (96.7 to 99.7)		
Week 20	98.5 (97.1 to 99.9)	97.8 (96.2 to 99.5)		
Week 24	98.6 (97.2 to 100.0)	97.5 (95.7 to 99.3)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	8.7 (5.5 to 11.9)	8.6 (5.5 to 11.8)		
Week 8	14.1 (10.3 to 18.0)	15.5 (11.5 to 19.5)		
Week 12	15.6 (11.7 to 19.6)	20.2 (15.7 to 24.6)		
Week 16	17.4 (13.3 to 21.6)	22.0 (17.4 to 26.5)		
Week 20	20.7 (16.2 to 25.2)	23.8 (19.0 to 28.5)		
Week 24	22.9 (18.2 to 27.6)	23.8 (19.1 to 28.5)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	55.6 (50.6 to 60.5)	62.3 (57.3 to 67.3)		
Week 8	63.9 (59.3 to 68.6)	70.3 (65.7 to 74.9)		
Week 12	69.0 (64.4 to 73.6)	69.2 (64.4 to 74.0)		
Week 16	72.2 (67.7 to 76.8)	72.1 (67.5 to 76.8)		
Week 20	73.3 (69.1 to 77.6)	76.1 (71.7 to 80.5)		
Week 24	73.7 (69.3 to 78.1)	76.5 (71.9 to 81.0)		

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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	3.6 (2.0 to 5.3)	1.5 (0.1 to 2.9)		
Week 8	3.2 (1.3 to 5.0)	1.9 (0.5 to 3.3)		
Week 12	2.3 (0.8 to 3.8)	1.5 (0.2 to 2.8)		
Week 16	2.3 (0.8 to 3.8)	1.9 (0.4 to 3.3)		
Week 20	2.3 (0.8 to 3.8)	1.9 (0.4 to 3.3)		
Week 24	2.3 (0.8 to 3.8)	1.9 (0.4 to 3.3)		

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 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 (≥55 and ≤54 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	276	277		
Units: microns				
arithmetic mean (confidence interval 95%)				
Week 4	-283.9 (-290.1 to -277.8)	-281.1 (-287.2 to -274.9)		
Week 8	-299.4 (-305.2 to -293.7)	-296.9 (-302.6 to -291.2)		
Week 12	-304.4 (-309.7 to -299.1)	-298.8 (-304.1 to -293.5)		

Week 16	-306.1 (-311.5 to -300.8)	-301.4 (-306.7 to -296.1)		
Week 20	-307.3 (-312.5 to -302.1)	-302.2 (-307.4 to -297.0)		
Week 24	-311.4 (-316.4 to -306.4)	-304.4 (-309.3 to -299.4)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	88.8 (85.1 to 92.5)	88.1 (84.4 to 91.9)		
Week 8	94.5 (91.9 to 97.2)	93.2 (90.3 to 96.1)		
Week 12	96.4 (94.2 to 98.5)	92.1 (89.0 to 95.2)		
Week 16	95.3 (92.8 to 97.7)	93.6 (90.7 to 96.4)		
Week 20	96.0 (93.7 to 98.3)	94.6 (92.1 to 97.2)		
Week 24	95.3 (92.8 to 97.7)	93.9 (91.2 to 96.6)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	46.1 (40.2 to 51.9)	54.8 (49.0 to 60.6)		
Week 8	53.8 (48.2 to 59.4)	57.4 (51.6 to 63.1)		
Week 12	65.3 (59.7 to 70.8)	56.6 (50.8 to 62.4)		
Week 16	69.9 (64.6 to 75.3)	72.9 (67.8 to 78.1)		
Week 20	67.1 (61.6 to 72.6)	66.4 (60.9 to 71.9)		
Week 24	72.5 (67.3 to 77.7)	66.0 (60.5 to 71.6)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	76.1 (71.1 to 81.1)	72.9 (67.8 to 78.1)		
Week 8	93.1 (90.2 to 96.1)	91.4 (88.1 to 94.6)		
Week 12	96.4 (94.2 to 98.6)	97.1 (95.2 to 99.1)		
Week 16	95.3 (92.8 to 97.8)	96.4 (94.2 to 98.6)		
Week 20	98.2 (96.6 to 99.8)	97.8 (96.1 to 99.5)		
Week 24	91.3 (88.0 to 94.6)	90.3 (86.9 to 93.7)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	37.8 (32.1 to 43.4)	40.8 (35.2 to 46.4)		
Week 8	50.9 (45.3 to 56.5)	54.1 (48.4 to 59.9)		
Week 12	63.8 (58.2 to 69.4)	56.3 (50.5 to 62.1)		
Week 16	67.1 (61.6 to 72.6)	72.6 (67.4 to 77.8)		
Week 20	66.0 (60.5 to 71.5)	66.0 (60.5 to 71.6)		
Week 24	66.3 (60.8 to 71.9)	61.0 (55.3 to 66.7)		

Statistical analyses

No statistical analyses for this end point

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 (≥55 and ≤54 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	276	277		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 4	11.5 (10.5 to 12.5)	12.4 (11.4 to 13.4)		
Week 8	13.7 (12.6 to 14.7)	15.1 (14.1 to 16.2)		
Week 12	15.1 (14.0 to 16.1)	15.9 (14.8 to 17.0)		
Week 16	15.5 (14.4 to 16.6)	16.5 (15.4 to 17.6)		
Week 20	16.3 (15.1 to 17.4)	17.2 (16.1 to 18.4)		
Week 24	16.8 (15.6 to 17.9)	17.5 (16.3 to 18.6)		
Week 28	16.5 (15.3 to 17.6)	17.3 (16.2 to 18.4)		
Week 32	17.2 (16.0 to 18.4)	17.5 (16.3 to 18.7)		
Week 36	17.3 (16.1 to 18.4)	18.0 (16.8 to 19.2)		
Week 40	17.3 (16.1 to 18.4)	17.7 (16.6 to 18.9)		
Week 44	18.1 (16.8 to 19.3)	17.7 (16.5 to 18.9)		
Week 48	18.0 (16.8 to 19.3)	18.2 (17.0 to 19.4)		
Week 52	18.0 (16.7 to 19.3)	18.4 (17.1 to 19.7)		
Week 56	17.3 (16.0 to 18.6)	18.1 (16.8 to 19.4)		
Week 60	18.0 (16.7 to 19.3)	18.6 (17.3 to 19.8)		
Week 64	17.9 (16.6 to 19.2)	18.6 (17.3 to 19.9)		
Week 68	18.1 (16.8 to 19.4)	18.8 (17.5 to 20.1)		
Week 72	18.4 (17.1 to 19.7)	18.8 (17.5 to 20.1)		

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	253	244		
Units: score on a scale				
arithmetic mean (confidence interval 95%)	5.6 (4.5 to 6.7)	5.9 (4.8 to 7.1)		

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	497
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Adjusted Means
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.76

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	34.3 (28.9 to 39.8)	36.9 (31.5 to 42.3)		
Week 8	41.2 (35.6 to 46.9)	46.7 (41.0 to 52.3)		
Week 12	51.0 (45.3 to 56.7)	52.1 (46.3 to 57.8)		
Week 16	53.6 (47.8 to 59.3)	56.4 (50.8 to 62.1)		
Week 20	56.1 (50.3 to 61.8)	58.9 (53.3 to 64.6)		
Week 24	56.1 (50.4 to 61.9)	60.4 (54.7 to 66.0)		
Week 28	55.8 (50.0 to 61.5)	61.8 (56.2 to 67.4)		
Week 32	59.0 (53.3 to 64.6)	61.4 (55.8 to 67.1)		
Week 36	61.2 (55.5 to 66.8)	62.5 (56.9 to 68.1)		
Week 40	60.8 (55.2 to 66.4)	61.1 (55.4 to 66.7)		
Week 44	65.5 (60.1 to 71.0)	58.9 (53.4 to 64.5)		
Week 48	64.1 (58.5 to 69.6)	60.7 (55.1 to 66.3)		
Week 52	61.2 (55.6 to 66.8)	64.0 (58.4 to 69.5)		
Week 56	57.9 (52.3 to 63.5)	63.6 (58.1 to 69.2)		
Week 60	62.6 (57.1 to 68.1)	62.9 (57.4 to 68.4)		
Week 64	61.9 (56.3 to 67.4)	65.4 (59.9 to 70.9)		
Week 68	63.0 (57.5 to 68.4)	64.7 (59.2 to 70.2)		
Week 72	62.3 (56.7 to 67.8)	66.9 (61.5 to 72.3)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	57.5 (51.8 to 63.3)	59.2 (53.6 to 64.9)		
Week 8	69.1 (63.8 to 74.5)	69.0 (63.6 to 74.4)		
Week 12	75.0 (69.9 to 80.1)	74.8 (69.7 to 79.8)		
Week 16	72.1 (66.9 to 77.3)	76.6 (71.6 to 81.5)		
Week 20	75.3 (70.3 to 80.4)	79.1 (74.3 to 83.9)		
Week 24	77.5 (72.6 to 82.4)	77.3 (72.4 to 82.2)		
Week 28	76.1 (71.1 to 81.1)	76.6 (71.6 to 81.5)		
Week 32	77.5 (72.6 to 82.4)	78.4 (73.6 to 83.2)		

Week 36	75.7 (70.7 to 80.7)	78.7 (74.0 to 83.5)		
Week 40	77.5 (72.7 to 82.4)	76.2 (71.3 to 81.2)		
Week 44	80.4 (75.8 to 85.1)	76.6 (71.7 to 81.5)		
Week 48	79.7 (75.0 to 84.4)	79.4 (74.7 to 84.2)		
Week 52	80.8 (76.2 to 85.4)	80.2 (75.5 to 84.8)		
Week 56	75.7 (70.7 to 80.7)	78.0 (73.2 to 82.9)		
Week 60	79.3 (74.6 to 84.0)	80.5 (75.9 to 85.2)		
Week 64	78.9 (74.2 to 83.7)	78.7 (73.9 to 83.5)		
Week 68	78.9 (74.2 to 83.7)	77.3 (72.4 to 82.2)		
Week 72	80.4 (75.8 to 85.0)	79.5 (74.7 to 84.2)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				

Week 4	75.7 (70.7 to 80.7)	79.1 (74.4 to 83.9)		
Week 8	84.0 (79.7 to 88.3)	88.1 (84.3 to 91.9)		
Week 12	87.0 (83.1 to 90.9)	87.0 (83.1 to 91.0)		
Week 16	85.9 (81.8 to 89.9)	88.8 (85.1 to 92.5)		
Week 20	88.4 (84.6 to 92.2)	90.3 (86.8 to 93.7)		
Week 24	90.9 (87.6 to 94.3)	89.6 (86.0 to 93.1)		
Week 28	89.1 (85.5 to 92.8)	87.8 (84.0 to 91.6)		
Week 32	89.5 (85.9 to 93.1)	87.7 (83.9 to 91.6)		
Week 36	88.4 (84.6 to 92.1)	90.6 (87.2 to 94.0)		
Week 40	90.2 (86.7 to 93.7)	90.6 (87.2 to 94.0)		
Week 44	89.1 (85.5 to 92.8)	88.4 (84.7 to 92.2)		
Week 48	88.4 (84.6 to 92.2)	90.3 (86.8 to 93.8)		
Week 52	89.9 (86.4 to 93.4)	88.5 (84.7 to 92.2)		
Week 56	88.0 (84.3 to 91.8)	87.0 (83.1 to 91.0)		
Week 60	89.9 (86.3 to 93.4)	88.1 (84.3 to 91.9)		
Week 64	90.6 (87.1 to 94.0)	87.7 (83.9 to 91.6)		
Week 68	89.5 (85.9 to 93.1)	87.1 (83.1 to 91.0)		
Week 72	89.8 (86.3 to 93.4)	87.4 (83.5 to 91.3)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	90.2 (86.8 to 93.6)	93.2 (90.3 to 96.1)		
Week 8	92.7 (89.7 to 95.8)	96.8 (94.7 to 98.8)		
Week 12	94.9 (92.4 to 97.5)	94.2 (91.5 to 97.0)		
Week 16	93.8 (91.1 to 96.6)	94.9 (92.4 to 97.5)		
Week 20	94.9 (92.4 to 97.5)	96.0 (93.8 to 98.3)		
Week 24	96.4 (94.2 to 98.6)	95.3 (92.9 to 97.8)		
Week 28	95.3 (92.9 to 97.8)	95.0 (92.4 to 97.5)		
Week 32	96.0 (93.8 to 98.3)	95.0 (92.4 to 97.5)		
Week 36	94.2 (91.5 to 96.9)	94.6 (92.0 to 97.2)		
Week 40	94.6 (91.9 to 97.2)	95.7 (93.3 to 98.0)		
Week 44	95.3 (92.9 to 97.7)	94.6 (92.0 to 97.2)		
Week 48	94.6 (92.0 to 97.2)	96.1 (93.8 to 98.3)		
Week 52	93.8 (91.1 to 96.6)	94.6 (92.1 to 97.2)		
Week 56	93.1 (90.2 to 96.1)	95.3 (92.9 to 97.8)		
Week 60	94.6 (91.9 to 97.2)	94.2 (91.5 to 97.0)		
Week 64	94.9 (92.4 to 97.5)	94.2 (91.5 to 97.0)		
Week 68	93.5 (90.6 to 96.4)	93.9 (91.1 to 96.7)		
Week 72	94.6 (91.9 to 97.2)	93.9 (91.1 to 96.7)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	99.3 (98.3 to 100.0)	98.9 (97.7 to 100.0)		
Week 8	99.3 (98.3 to 100.0)	98.9 (97.7 to 100.0)		
Week 12	99.3 (98.3 to 100.0)	98.9 (97.7 to 100.0)		
Week 16	99.3 (98.3 to 100.0)	98.6 (97.2 to 99.9)		
Week 20	99.6 (98.9 to 100.0)	98.6 (97.2 to 99.9)		
Week 24	99.6 (98.9 to 100.0)	98.6 (97.2 to 99.9)		
Week 28	99.6 (98.9 to 100.0)	98.6 (97.2 to 99.9)		
Week 32	99.6 (98.9 to 100.0)	98.6 (97.2 to 99.9)		
Week 36	99.6 (98.9 to 100.0)	98.6 (97.2 to 100.0)		
Week 40	98.9 (97.7 to 100.0)	98.6 (97.2 to 100.0)		
Week 44	99.3 (98.3 to 100.0)	98.6 (97.2 to 100.0)		
Week 48	99.3 (98.3 to 100.0)	98.2 (96.7 to 99.8)		
Week 52	98.6 (97.2 to 100.0)	98.2 (96.7 to 99.8)		
Week 56	98.9 (97.7 to 100.0)	98.2 (96.7 to 99.8)		
Week 60	99.3 (98.3 to 100.0)	98.2 (96.7 to 99.8)		

Week 64	98.9 (97.7 to 100.0)	97.9 (96.2 to 99.5)		
Week 68	98.9 (97.7 to 100.0)	98.2 (96.7 to 99.8)		
Week 72	98.9 (97.7 to 100.0)	98.2 (96.7 to 99.8)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	98.5 (97.1 to 99.9)	98.9 (97.7 to 100.0)		
Week 8	98.5 (97.1 to 100.0)	98.9 (97.7 to 100.0)		
Week 12	98.5 (97.1 to 99.9)	98.9 (97.7 to 100.0)		
Week 16	98.5 (97.1 to 99.9)	98.2 (96.7 to 99.7)		
Week 20	99.3 (98.3 to 100.0)	98.6 (97.2 to 99.9)		
Week 24	99.6 (98.9 to 100.0)	98.2 (96.7 to 99.7)		
Week 28	99.6 (98.9 to 100.0)	98.2 (96.7 to 99.7)		

Week 32	99.3 (98.3 to 100.0)	98.2 (96.7 to 99.7)		
Week 36	99.6 (98.9 to 100.0)	98.6 (97.2 to 100.0)		
Week 40	98.9 (97.7 to 100.0)	98.6 (97.2 to 100.0)		
Week 44	99.3 (98.3 to 100.0)	98.2 (96.7 to 99.8)		
Week 48	98.9 (97.7 to 100.0)	98.2 (96.7 to 99.8)		
Week 52	98.6 (97.2 to 100.0)	98.2 (96.7 to 99.8)		
Week 56	98.9 (97.7 to 100.0)	97.9 (96.2 to 99.5)		
Week 60	98.9 (97.7 to 100.0)	98.2 (96.7 to 99.8)		
Week 64	98.6 (97.2 to 99.9)	97.1 (95.2 to 99.1)		
Week 68	98.6 (97.2 to 100.0)	97.9 (96.2 to 99.5)		
Week 72	98.2 (96.6 to 99.8)	97.9 (96.2 to 99.5)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				

number (confidence interval 95%)				
Week 4	97.1 (95.1 to 99.1)	98.6 (97.2 to 99.9)		
Week 8	97.8 (96.1 to 99.5)	98.6 (97.2 to 99.9)		
Week 12	97.8 (96.1 to 99.5)	98.9 (97.7 to 100.0)		
Week 16	97.8 (96.1 to 99.5)	98.2 (96.7 to 99.7)		
Week 20	98.5 (97.1 to 99.9)	97.8 (96.2 to 99.5)		
Week 24	98.6 (97.2 to 100.0)	97.5 (95.7 to 99.3)		
Week 28	98.2 (96.6 to 99.8)	97.5 (95.7 to 99.3)		
Week 32	98.6 (97.2 to 99.9)	97.8 (96.2 to 99.5)		
Week 36	98.2 (96.7 to 99.7)	97.5 (95.7 to 99.3)		
Week 40	97.1 (95.2 to 99.0)	97.5 (95.6 to 99.3)		
Week 44	98.6 (97.2 to 99.9)	97.8 (96.1 to 99.5)		
Week 48	97.1 (95.2 to 99.0)	97.9 (96.2 to 99.5)		
Week 52	97.1 (95.2 to 99.1)	97.5 (95.7 to 99.3)		
Week 56	97.5 (95.6 to 99.3)	97.5 (95.7 to 99.3)		
Week 60	97.8 (96.1 to 99.5)	96.8 (94.7 to 98.8)		
Week 64	97.1 (95.1 to 99.1)	96.8 (94.7 to 98.8)		
Week 68	97.1 (95.1 to 99.1)	97.1 (95.2 to 99.1)		
Week 72	97.1 (95.1 to 99.1)	96.8 (94.7 to 98.8)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	8.7 (5.5 to 11.9)	8.6 (5.5 to 11.8)		
Week 8	14.1 (10.3 to 18.0)	15.5 (11.5 to 19.5)		
Week 12	15.6 (11.7 to 19.6)	20.2 (15.7 to 24.6)		
Week 16	17.4 (13.3 to 21.6)	22.0 (17.4 to 26.5)		
Week 20	20.7 (16.2 to 25.2)	23.8 (19.0 to 28.5)		
Week 24	22.9 (18.2 to 27.6)	23.8 (19.1 to 28.5)		
Week 28	24.0 (19.2 to 28.8)	25.6 (20.7 to 30.4)		
Week 32	25.1 (20.3 to 29.8)	23.4 (18.8 to 28.0)		
Week 36	25.1 (20.2 to 29.9)	25.2 (20.4 to 30.0)		
Week 40	26.9 (22.0 to 31.8)	22.0 (17.4 to 26.5)		
Week 44	26.8 (21.8 to 31.8)	24.8 (20.0 to 29.7)		
Week 48	29.0 (24.0 to 34.1)	25.2 (20.3 to 30.1)		
Week 52	26.8 (21.9 to 31.7)	25.6 (20.7 to 30.4)		
Week 56	26.1 (21.2 to 31.0)	22.0 (17.3 to 26.6)		
Week 60	27.6 (22.6 to 32.6)	25.6 (20.8 to 30.4)		
Week 64	30.1 (25.0 to 35.3)	24.5 (19.7 to 29.3)		
Week 68	29.4 (24.2 to 34.6)	25.9 (21.0 to 30.8)		
Week 72	29.4 (24.3 to 34.5)	24.8 (20.0 to 29.7)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	55.6 (50.6 to 60.5)	62.3 (57.3 to 67.3)		
Week 8	63.9 (59.3 to 68.6)	70.3 (65.7 to 74.9)		
Week 12	69.0 (64.4 to 73.6)	69.2 (64.4 to 74.0)		
Week 16	72.2 (67.7 to 76.8)	72.1 (67.5 to 76.8)		
Week 20	73.3 (69.1 to 77.6)	76.1 (71.7 to 80.5)		
Week 24	73.7 (69.3 to 78.1)	76.5 (71.9 to 81.0)		
Week 28	73.3 (68.7 to 77.9)	75.4 (70.7 to 80.0)		
Week 32	76.9 (72.6 to 81.2)	75.4 (70.7 to 80.1)		
Week 36	76.2 (71.8 to 80.6)	77.9 (73.3 to 82.5)		
Week 40	75.5 (71.0 to 79.9)	76.8 (72.3 to 81.3)		
Week 44	76.9 (72.4 to 81.4)	76.1 (71.4 to 80.7)		
Week 48	77.2 (72.7 to 81.8)	79.3 (75.0 to 83.7)		
Week 52	78.7 (74.3 to 83.1)	80.4 (76.1 to 84.7)		
Week 56	76.2 (71.5 to 80.9)	79.0 (74.5 to 83.5)		

Week 60	80.2 (75.8 to 84.5)	79.0 (74.5 to 83.5)		
Week 64	77.6 (73.0 to 82.2)	81.1 (76.8 to 85.5)		
Week 68	77.6 (73.0 to 82.2)	80.4 (76.0 to 84.9)		
Week 72	78.0 (73.5 to 82.4)	79.0 (74.4 to 83.6)		

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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	3.6 (2.0 to 5.3)	1.5 (0.1 to 2.9)		
Week 8	3.2 (1.3 to 5.0)	1.9 (0.5 to 3.3)		
Week 12	2.3 (0.8 to 3.8)	1.5 (0.2 to 2.8)		
Week 16	2.3 (0.8 to 3.8)	1.9 (0.4 to 3.3)		
Week 20	2.3 (0.8 to 3.8)	1.9 (0.4 to 3.3)		
Week 24	2.3 (0.8 to 3.8)	1.9 (0.4 to 3.3)		
Week 28	2.0 (0.6 to 3.5)	1.9 (0.4 to 3.3)		
Week 32	2.4 (0.8 to 4.0)	1.9 (0.4 to 3.3)		
Week 36	1.9 (0.5 to 3.4)	1.5 (0.2 to 2.8)		
Week 40	2.3 (0.8 to 3.7)	1.5 (0.2 to 2.8)		
Week 44	2.7 (1.0 to 4.4)	1.5 (0.2 to 2.8)		

Week 48	2.4 (0.8 to 4.0)	2.2 (0.6 to 3.9)		
Week 52	3.1 (1.3 to 4.9)	2.6 (0.9 to 4.3)		
Week 56	2.7 (1.0 to 4.4)	2.6 (0.9 to 4.3)		
Week 60	2.1 (0.6 to 3.6)	2.6 (0.9 to 4.3)		
Week 64	3.1 (1.3 to 4.9)	2.2 (0.6 to 3.9)		
Week 68	2.1 (0.6 to 3.6)	1.8 (0.3 to 3.3)		
Week 72	2.1 (0.6 to 3.6)	2.2 (0.5 to 3.9)		

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 and 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	276	277		
Units: score on a scale				
arithmetic mean (confidence interval 95%)				
Week 24	5.6 (4.5 to 6.6)	5.9 (4.9 to 7.0)		
Week 48	6.4 (5.3 to 7.5)	6.3 (5.2 to 7.4)		
Week 72	6.0 (4.8 to 7.3)	7.8 (6.6 to 9.0)		

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 (≥55 and ≤54 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	276	277		
Units: microns				
arithmetic mean (confidence interval 95%)				
Week 4	-287.3 (-293.5 to -281.1)	-284.3 (-290.4 to -278.2)		
Week 8	-302.9 (-308.7 to -297.2)	-300.2 (-306.0 to -294.5)		
Week 12	-307.8 (-313.1 to -302.6)	-301.9 (-307.1 to -296.7)		
Week 16	-309.3 (-314.6 to -304.0)	-304.5 (-309.8 to -299.3)		
Week 20	-310.6 (-315.5 to -305.6)	-304.2 (-309.1 to -299.3)		
Week 24	-314.5 (-319.5 to -309.6)	-307.6 (-312.5 to -302.7)		
Week 28	-294.0 (-302.2 to -285.8)	-285.1 (-293.3 to -276.9)		
Week 32	-308.3 (-314.6 to -302.0)	-303.2 (-309.4 to -297.0)		
Week 36	-304.1 (-310.6 to -297.6)	-298.8 (-305.2 to -292.4)		
Week 40	-296.7 (-304.4 to -288.9)	-285.8 (-293.7 to -278.0)		
Week 44	-309.2 (-315.9 to -302.5)	-301.6 (-308.3 to -294.9)		
Week 48	-309.4 (-315.3 to -303.5)	-302.8 (-308.7 to -296.9)		
Week 52	-302.2 (-308.6 to -295.7)	-302.4 (-308.8 to -296.0)		
Week 56	-294.0 (-302.6 to -285.5)	-288.0 (-296.6 to -279.4)		

Week 60	-309.5 (-315.1 to -303.9)	-306.2 (-311.9 to -300.6)		
Week 64	-311.1 (-316.3 to -305.9)	-305.9 (-311.1 to -300.7)		
Week 68	-311.2 (-316.3 to -306.1)	-307.9 (-313.0 to -302.8)		
Week 72	-310.5 (-315.7 to -305.4)	-307.2 (-312.3 to -302.0)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	88.8 (85.1 to 92.5)	88.1 (84.4 to 91.9)		
Week 8	94.5 (91.9 to 97.2)	93.2 (90.3 to 96.1)		
Week 12	96.4 (94.2 to 98.5)	92.1 (89.0 to 95.2)		
Week 16	95.3 (92.8 to 97.7)	93.6 (90.7 to 96.4)		
Week 20	96.0 (93.7 to 98.3)	94.6 (92.1 to 97.2)		
Week 24	95.6 (93.3 to 98.0)	94.3 (91.6 to 96.9)		

Week 28	89.1 (85.5 to 92.8)	86.0 (82.0 to 90.0)		
Week 32	94.6 (91.9 to 97.2)	92.5 (89.4 to 95.5)		
Week 36	93.8 (91.1 to 96.5)	90.7 (87.3 to 94.0)		
Week 40	89.5 (85.9 to 93.0)	84.2 (79.9 to 88.4)		
Week 44	96.0 (93.7 to 98.3)	92.1 (88.9 to 95.2)		
Week 48	94.9 (92.4 to 97.5)	91.4 (88.1 to 94.6)		
Week 52	92.4 (89.3 to 95.5)	91.4 (88.2 to 94.6)		
Week 56	89.5 (85.9 to 93.1)	86.3 (82.3 to 90.3)		
Week 60	94.2 (91.5 to 96.9)	93.9 (91.1 to 96.7)		
Week 64	95.3 (92.8 to 97.8)	93.9 (91.1 to 96.7)		
Week 68	94.9 (92.4 to 97.5)	92.4 (89.4 to 95.5)		
Week 72	94.2 (91.5 to 96.9)	94.2 (91.5 to 97.0)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				

number (confidence interval 95%)				
Week 4	46.1 (40.2 to 51.9)	54.8 (49.0 to 60.6)		
Week 8	53.8 (48.2 to 59.4)	57.4 (51.6 to 63.1)		
Week 12	65.3 (59.7 to 70.8)	56.6 (50.8 to 62.4)		
Week 16	69.9 (64.6 to 75.3)	72.9 (67.8 to 78.1)		
Week 20	67.1 (61.6 to 72.6)	66.4 (60.9 to 71.9)		
Week 24	73.9 (68.9 to 79.0)	69.3 (63.9 to 74.7)		
Week 28	54.4 (48.7 to 60.2)	47.6 (41.8 to 53.5)		
Week 32	68.1 (62.6 to 73.6)	65.0 (59.4 to 70.6)		
Week 36	60.9 (55.1 to 66.6)	56.0 (50.2 to 61.7)		
Week 40	50.8 (45.0 to 56.6)	48.1 (42.3 to 53.9)		
Week 44	70.3 (64.9 to 75.6)	63.9 (58.3 to 69.6)		
Week 48	76.1 (71.1 to 81.1)	67.9 (62.5 to 73.3)		
Week 52	55.8 (50.0 to 61.7)	56.7 (50.9 to 62.5)		
Week 56	58.4 (52.6 to 64.1)	58.9 (53.2 to 64.6)		
Week 60	75.0 (69.9 to 80.1)	72.6 (67.4 to 77.7)		
Week 64	75.8 (70.9 to 80.7)	69.7 (64.3 to 75.1)		
Week 68	69.9 (64.5 to 75.3)	68.6 (63.2 to 74.1)		
Week 72	72.8 (67.6 to 78.0)	72.9 (67.7 to 78.1)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	76.1 (71.1 to 81.1)	72.9 (67.8 to 78.1)		
Week 8	93.1 (90.2 to 96.1)	91.4 (88.1 to 94.6)		
Week 12	96.4 (94.2 to 98.6)	97.1 (95.2 to 99.1)		
Week 16	95.3 (92.8 to 97.8)	96.4 (94.2 to 98.6)		
Week 20	98.2 (96.6 to 99.8)	97.8 (96.1 to 99.5)		
Week 24	91.3 (88.0 to 94.6)	90.3 (86.9 to 93.7)		
Week 28	93.5 (90.7 to 96.4)	91.0 (87.6 to 94.3)		
Week 32	96.4 (94.2 to 98.6)	97.1 (95.2 to 99.1)		
Week 36	97.1 (95.1 to 99.1)	96.0 (93.7 to 98.3)		
Week 40	96.8 (94.7 to 98.8)	95.7 (93.3 to 98.1)		
Week 44	97.5 (95.7 to 99.3)	95.7 (93.3 to 98.0)		
Week 48	97.1 (95.1 to 99.1)	94.6 (91.9 to 97.2)		
Week 52	98.2 (96.6 to 99.8)	97.1 (95.2 to 99.1)		
Week 56	95.3 (92.8 to 97.8)	95.0 (92.4 to 97.5)		
Week 60	95.7 (93.3 to 98.1)	96.0 (93.8 to 98.3)		
Week 64	98.2 (96.7 to 99.7)	96.8 (94.7 to 98.8)		
Week 68	97.5 (95.6 to 99.3)	97.5 (95.7 to 99.3)		
Week 72	96.4 (94.2 to 98.6)	94.9 (92.4 to 97.5)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4	37.8 (32.1 to 43.4)	40.8 (35.2 to 46.4)		
Week 8	50.9 (45.3 to 56.5)	54.1 (48.4 to 59.9)		
Week 12	63.8 (58.2 to 69.4)	56.3 (50.5 to 62.1)		
Week 16	67.1 (61.6 to 72.6)	72.6 (67.4 to 77.8)		
Week 20	66.0 (60.5 to 71.5)	66.0 (60.5 to 71.6)		
Week 24	67.4 (61.9 to 72.9)	64.3 (58.6 to 69.9)		
Week 28	53.0 (47.2 to 58.7)	46.9 (41.1 to 52.8)		
Week 32	67.4 (61.9 to 72.9)	64.6 (59.0 to 70.2)		
Week 36	60.5 (54.8 to 66.3)	54.2 (48.4 to 59.9)		
Week 40	50.4 (44.6 to 56.2)	47.3 (41.5 to 53.2)		
Week 44	69.6 (64.2 to 74.9)	63.6 (57.9 to 69.2)		
Week 48	74.7 (69.6 to 79.8)	65.4 (59.8 to 70.9)		
Week 52	55.5 (49.6 to 61.3)	55.6 (49.8 to 61.4)		
Week 56	58.0 (52.2 to 63.8)	57.8 (52.0 to 63.6)		
Week 60	73.9 (68.8 to 79.1)	70.4 (65.1 to 75.7)		
Week 64	75.4 (70.5 to 80.4)	69.3 (64.0 to 74.7)		
Week 68	68.9 (63.4 to 74.3)	68.3 (62.8 to 73.7)		

Week 72	70.7 (65.3 to 76.0)	71.1 (65.8 to 76.4)		

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 (≥55 and ≤54 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	276	277		
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 28	-0.3 (-0.8 to 0.3)	-0.1 (-0.6 to 0.5)		
Week 32	0.5 (-0.1 to 1.0)	0.0 (-0.6 to 0.5)		
Week 36	0.5 (-0.2 to 1.2)	0.6 (-0.1 to 1.2)		
Week 40	0.3 (-0.4 to 1.1)	0.4 (-0.3 to 1.2)		
Week 44	1.1 (0.3 to 1.9)	0.3 (-0.5 to 1.1)		
Week 48	1.1 (0.3 to 2.0)	0.7 (-0.1 to 1.6)		
Week 52	1.1 (0.2 to 2.0)	0.9 (0.0 to 1.8)		
Week 56	0.4 (-0.5 to 1.4)	0.6 (-0.3 to 1.6)		
Week 60	1.0 (0.1 to 2.0)	1.1 (0.1 to 2.0)		

Week 64	0.9 (0.0 to 1.9)	1.2 (0.2 to 2.2)		
Week 68	1.2 (0.2 to 2.1)	1.3 (0.4 to 2.2)		
Week 72	1.5 (0.5 to 2.5)	1.3 (0.3 to 2.3)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	85.5 (81.4 to 89.6)	84.1 (79.8 to 88.3)		
Week 32	89.1 (85.5 to 92.7)	87.7 (83.9 to 91.5)		
Week 36	89.5 (85.9 to 93.1)	88.4 (84.7 to 92.2)		
Week 40	89.5 (85.9 to 93.0)	88.0 (84.2 to 91.8)		
Week 44	89.9 (86.3 to 93.4)	86.3 (82.2 to 90.3)		
Week 48	89.5 (85.9 to 93.1)	86.6 (82.6 to 90.6)		
Week 52	89.9 (86.3 to 93.4)	87.7 (83.9 to 91.6)		
Week 56	88.0 (84.3 to 91.8)	86.6 (82.6 to 90.6)		

Week 60	88.8 (85.1 to 92.5)	87.0 (83.0 to 90.9)		
Week 64	89.5 (85.9 to 93.1)	86.6 (82.6 to 90.6)		
Week 68	88.4 (84.7 to 92.1)	87.0 (83.0 to 90.9)		
Week 72	88.4 (84.7 to 92.1)	87.0 (83.0 to 90.9)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	84.8 (80.6 to 89.0)	82.3 (77.8 to 86.7)		
Week 32	88.8 (85.1 to 92.5)	85.9 (81.8 to 89.9)		
Week 36	87.3 (83.4 to 91.2)	87.0 (83.0 to 90.9)		
Week 40	87.7 (83.8 to 91.5)	86.3 (82.2 to 90.3)		
Week 44	88.8 (85.1 to 92.5)	85.5 (81.4 to 89.7)		
Week 48	88.4 (84.7 to 92.2)	85.2 (81.0 to 89.3)		

Week 52	88.4 (84.7 to 92.2)	85.2 (81.0 to 89.3)		
Week 56	86.2 (82.2 to 90.2)	83.4 (79.0 to 87.7)		
Week 60	86.9 (83.0 to 90.9)	83.4 (79.0 to 87.7)		
Week 64	86.9 (83.0 to 90.9)	85.2 (81.0 to 89.4)		
Week 68	86.6 (82.6 to 90.6)	85.5 (81.4 to 89.7)		
Week 72	86.6 (82.6 to 90.6)	85.5 (81.4 to 89.7)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	74.6 (69.5 to 79.7)	73.6 (68.5 to 78.8)		
Week 32	80.0 (75.4 to 84.7)	77.2 (72.3 to 82.1)		
Week 36	79.7 (75.0 to 84.4)	79.0 (74.2 to 83.8)		
Week 40	78.6 (73.8 to 83.4)	78.3 (73.5 to 83.1)		

Week 44	83.3 (79.0 to 87.7)	76.9 (71.9 to 81.9)		
Week 48	82.6 (78.2 to 87.0)	79.4 (74.6 to 84.1)		
Week 52	81.5 (77.0 to 86.0)	79.4 (74.6 to 84.1)		
Week 56	76.4 (71.5 to 81.3)	78.3 (73.5 to 83.1)		
Week 60	79.0 (74.2 to 83.7)	77.2 (72.3 to 82.1)		
Week 64	77.9 (73.0 to 82.8)	76.1 (71.1 to 81.1)		
Week 68	78.2 (73.4 to 83.1)	76.5 (71.6 to 81.5)		
Week 72	77.5 (72.7 to 82.4)	77.6 (72.7 to 82.5)		

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 (≥55 and ≤54 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	276	277		
Units: Percentage of participants				
number (confidence interval 95%)				
Week 28	46.4 (40.6 to 52.3)	51.3 (45.4 to 57.1)		
Week 32	55.4 (49.6 to 61.2)	54.2 (48.3 to 60.0)		

Week 36	55.1 (49.2 to 60.9)	52.7 (46.9 to 58.6)		
Week 40	56.2 (50.4 to 62.0)	55.2 (49.4 to 61.1)		
Week 44	62.4 (56.7 to 68.0)	56.0 (50.1 to 61.8)		
Week 48	63.8 (58.2 to 69.4)	56.6 (50.9 to 62.4)		
Week 52	59.8 (54.1 to 65.5)	58.5 (52.7 to 64.3)		
Week 56	57.2 (51.5 to 63.0)	57.4 (51.5 to 63.2)		
Week 60	58.0 (52.1 to 63.8)	60.3 (54.5 to 66.0)		
Week 64	62.0 (56.3 to 67.7)	56.6 (50.8 to 62.5)		
Week 68	60.9 (55.1 to 66.6)	58.8 (53.1 to 64.6)		
Week 72	63.0 (57.4 to 68.7)	58.1 (52.3 to 63.9)		

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	248	244		
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 4 Weeks (Q4W)	22.6 (17.4 to 27.8)	25.0 (19.6 to 30.4)		
Once Every 8 Weeks (Q8W)	13.3 (9.1 to 17.5)	18.0 (13.2 to 22.9)		

Once Every 12 Weeks (Q12W)	11.7 (7.7 to 15.7)	9.4 (5.8 to 13.1)		
Once Every 16 Weeks (Q16W)	52.4 (46.2 to 58.6)	47.5 (41.3 to 53.8)		

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	270	267		
Units: Injections				
median (full range (min-max))	4.0 (1 to 12)	4.0 (1 to 12)		

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 (Part 1)	Arm B: Aflibercept Q4W (Part 1)	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	Subject analysis set	Subject analysis set
Number of subjects analysed	276	274	270	267
Units: Participants				
Adverse Event (AE)	45	56	76	81
AE by Severity: Mild	40	47	50	64
AE by Severity: Moderate	4	8	25	16
AE by Severity: Severe	0	1	1	1
AE by Severity: Missing	1	0	0	0
Serious Adverse Event (SAE)	3	2	4	3
AE Leading to Withdrawal from Study Treatment	0	0	0	1
Treatment Related AEs	1	3	7	8
Treatment Related SAEs	0	0	0	0
Any AE of Special Interest (AESI)	1	2	1	1
AESI: Drop in Visual Acuity Score ≥30	1	2	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 (Part 1)	Arm B: Aflibercept Q4W (Part 1)	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	Subject analysis set	Subject analysis set
Number of subjects analysed	276	274	270	267
Units: Participants				
Adverse Event (AE)	94	99	136	126
Serious Adverse Event (SAE)	9	16	25	23
AE Leading to Withdrawal from Study Treatment	1	0	0	3
Any AE of Special Interest (AESI)	0	0	0	0

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 (Part 1)	Arm B: Aflibercept Q4W (Part 1)	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	Subject analysis set	Subject analysis set
Number of subjects analysed	276	274	270	267
Units: Participants				
Adverse Event (AE)	25	21	37	30
Serious Adverse Event (SAE)	0	0	0	0
Any AE of Special Interest (AESI)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Faricimab Over Time

End point title	Plasma Concentration of Faricimab Over Time

End point description:

Pharmacokinetic-Evaluable Population: All safety- evaluable participants randomized to faricimab arm or who received faricimab with at least one plasma sample, provided sufficient dosing information (dose and dosing time) is available. The number analyzed indicates all participants who provided a PK sample at a given timepoint. The values '999999' indicate that 0 participants provided samples at that timepoint, and therefore, there were no results to report.

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	276	268		
Units: microgram per millilitre (µg/mL)				
arithmetic mean (standard deviation)				
Baseline (n = 273, 0)	0.0000 (± 0.0000)	999999 (± 999999)		
Week 4 (n = 264, 0)	0.0215 (± 0.0160)	999999 (± 999999)		
Week 24 (n = 247, 241)	0.0220 (± 0.0181)	0.0005 (± 0.0006)		
Week 28 (n = 238, 242)	0.0040 (± 0.0072)	0.0025 (± 0.077)		
Week 52 (n = 231, 224)	0.0061 (± 0.0110)	0.0097 (± 0.0156)		
Week 72 (n = 231, 229)	0.0076 (± 0.0109)	0.0087 (± 0.0146)		

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	274	266	540	
Units: Participants				
Baseline (BL): Total ADA-Positive	3	4	7	
Post-BL: Total ADA-Positive	33	23	56	
Post-BL: Treatment-Emergent ADA-Positive	32	21	53	
Post-BL: Treatment-Unaffected ADA-Positive	1	2	3	

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 were to receive faricimab 6 milligrams (mg) administered by intravitreal (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 were to receive aflibercept 2 milligrams (mg) administered by intravitreal (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	12 / 276 (4.35%)	26 / 267 (9.74%)	29 / 270 (10.74%)
number of deaths (all causes)	1	2	1
number of deaths resulting from adverse events	1	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			

subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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
Breast cancer			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer metastatic			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Pancreatic neoplasm			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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 metastatic			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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 recurrent			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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			
Shoulder arthroplasty			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Death			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular stent stenosis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	1 / 276 (0.36%)	0 / 267 (0.00%)	0 / 270 (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
Urogenital prolapse			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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
Cervical polyp			
subjects affected / exposed	1 / 276 (0.36%)	0 / 267 (0.00%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Acute pulmonary oedema			

subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Product issues			
Device malfunction			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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			
Fall			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 276 (0.36%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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
Sternal fracture			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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 / 276 (0.00%)	0 / 267 (0.00%)	2 / 270 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Comminuted fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burns third degree			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Ulna fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Vertebral artery hypoplasia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Myocardial infarction			
subjects affected / exposed	1 / 276 (0.36%)	1 / 267 (0.37%)	2 / 270 (0.74%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Coronary artery disease			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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
Angina pectoris			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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
Angina unstable			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	2 / 270 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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
Cerebral infarction			

subjects affected / exposed	3 / 276 (1.09%)	1 / 267 (0.37%)	0 / 270 (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
Multiple sclerosis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 276 (0.36%)	2 / 267 (0.75%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral thrombosis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Hypertensive encephalopathy			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 276 (0.00%)	2 / 267 (0.75%)	0 / 270 (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
Sciatica			

subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Eye disorders			
Vitreous haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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 vein occlusion	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 276 (0.36%)	0 / 267 (0.00%)	0 / 270 (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
Retinal ischaemia	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 276 (0.72%)	2 / 267 (0.75%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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 ischaemia	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tractional retinal detachment	Additional description: AEs occurred in the study eye		

subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular vascular disorder	Additional description: AEs occurred in the fellow eye		
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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 haemorrhage			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	1 / 276 (0.36%)	0 / 267 (0.00%)	0 / 270 (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
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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			
Glomerulonephritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Chronic kidney disease			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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 mass			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			

subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	2 / 270 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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			
Gastroenteritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	0 / 270 (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
COVID-19			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal sepsis			

subjects affected / exposed	0 / 276 (0.00%)	1 / 267 (0.37%)	0 / 270 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
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 infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 276 (0.36%)	0 / 267 (0.00%)	0 / 270 (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
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 276 (0.00%)	0 / 267 (0.00%)	1 / 270 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	17 / 274 (6.20%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pancreatic carcinoma			
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			

subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer metastatic				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic neoplasm				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer metastatic				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer recurrent				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Shoulder arthroplasty				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pain				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Vascular stent stenosis				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Uterine polyp				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urogenital prolapse				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical polyp				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute pulmonary oedema				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device malfunction			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sternal fracture			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Femur fracture				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Comminuted fracture				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Burns third degree				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ulna fracture				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Vertebral artery hypoplasia				
subjects affected / exposed	0 / 274 (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	2 / 274 (0.73%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	2 / 274 (0.73%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			

Atrial fibrillation				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arteriosclerosis coronary artery				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Carotid artery stenosis				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple sclerosis				

subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral thrombosis				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haematoma				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive encephalopathy				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intracranial aneurysm				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo positional				

subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Vitreous haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal vein occlusion	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 274 (0.36%)		
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	0 / 274 (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 study eye		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Macular ischaemia	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tractional retinal detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhegmatogenous retinal detachment	Additional description: AEs occurred in the study eye		

subjects affected / exposed	0 / 274 (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 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ocular vascular disorder	Additional description: AEs occurred in the fellow eye		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Skin ulcer				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Glomerulonephritis				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal mass				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Intervertebral disc protrusion				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Spinal osteoarthritis				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Gastroenteritis				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19 pneumonia				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	1 / 274 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal sepsis				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 274 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				

subjects affected / exposed	0 / 274 (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 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 274 (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	62 / 276 (22.46%)	87 / 267 (32.58%)	92 / 270 (34.07%)
Investigations			
Intraocular pressure increased	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 276 (0.36%)	8 / 267 (3.00%)	13 / 270 (4.81%)
occurrences (all)	2	11	21
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 276 (7.25%)	8 / 267 (3.00%)	14 / 270 (5.19%)
occurrences (all)	21	8	14
Eye disorders			
Dry eye	Additional description: AEs occurred in the study eye		
subjects affected / exposed	5 / 276 (1.81%)	4 / 267 (1.50%)	4 / 270 (1.48%)
occurrences (all)	5	4	5
Conjunctival haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	8 / 276 (2.90%)	10 / 267 (3.75%)	11 / 270 (4.07%)
occurrences (all)	9	11	11
Macular oedema	Additional description: AEs occurred in the study eye		

subjects affected / exposed	1 / 276 (0.36%)	5 / 267 (1.87%)	10 / 270 (3.70%)
occurrences (all)	1	8	11
Retinal vein occlusion	Additional description: AEs occurred in the study eye		
subjects affected / exposed	0 / 276 (0.00%)	8 / 267 (3.00%)	9 / 270 (3.33%)
occurrences (all)	0	10	12
Vitreous detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	4 / 276 (1.45%)	9 / 267 (3.37%)	7 / 270 (2.59%)
occurrences (all)	4	9	7
Cataract	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 276 (0.72%)	9 / 267 (3.37%)	9 / 270 (3.33%)
occurrences (all)	2	9	9
Vitreous floaters	Additional description: AEs occurred in the study eye		
subjects affected / exposed	7 / 276 (2.54%)	9 / 267 (3.37%)	0 / 270 (0.00%)
occurrences (all)	7	9	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 276 (0.72%)	4 / 267 (1.50%)	5 / 270 (1.85%)
occurrences (all)	2	4	6
Infections and infestations			
COVID-19			
subjects affected / exposed	10 / 276 (3.62%)	25 / 267 (9.36%)	32 / 270 (11.85%)
occurrences (all)	10	25	32
Upper respiratory tract infection			
subjects affected / exposed	4 / 276 (1.45%)	9 / 267 (3.37%)	6 / 270 (2.22%)
occurrences (all)	4	11	8
Nasopharyngitis			
subjects affected / exposed	6 / 276 (2.17%)	10 / 267 (3.75%)	7 / 270 (2.59%)
occurrences (all)	6	12	8

Non-serious adverse events	Arm B: Aflibercept Q4W (Part 1)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 274 (25.18%)		
Investigations			
Intraocular pressure increased	Additional description: AEs occurred in the study eye		
subjects affected / exposed	8 / 274 (2.92%)		
occurrences (all)	8		

Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 274 (2.55%)		
occurrences (all)	7		
Eye disorders			
Dry eye	Additional description: AEs occurred in the study eye		
subjects affected / exposed	9 / 274 (3.28%)		
occurrences (all)	9		
Conjunctival haemorrhage	Additional description: AEs occurred in the study eye		
subjects affected / exposed	10 / 274 (3.65%)		
occurrences (all)	11		
Macular oedema	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Retinal vein occlusion	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	3		
Vitreous detachment	Additional description: AEs occurred in the study eye		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Cataract	Additional description: AEs occurred in the study eye		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Vitreous floaters	Additional description: AEs occurred in the study eye		
subjects affected / exposed	6 / 274 (2.19%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 274 (3.65%)		
occurrences (all)	10		
Infections and infestations			
COVID-19			
subjects affected / exposed	16 / 274 (5.84%)		
occurrences (all)	16		
Upper respiratory tract infection			

subjects affected / exposed	5 / 274 (1.82%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	6 / 274 (2.19%)		
occurrences (all)	6		

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 protocol version 1 were: -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.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported