Clinical trial results:
A Phase III, Multicenter, Randomized, Double-Masked, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of Faricimab (RO6867461) in Patients with Diabetic Macular Edema (RHINE)

Summary

EudraCT number	2017-005105-12
Trial protocol	PT HU DE CZ GB DK ES IT
Global end of trial date	27 August 2021

Results information

Result version number	v1 (current)
This version publication date	02 September 2022
First version publication date	02 September 2022

Trial information

Trial identification

Sponsor protocol code	GR40398

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03622593
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche, Ltd.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland,
Public contact	F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 October 2020
Global end of trial reached?	Yes
Global end of trial date	27 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy of intravitreal (IVT) injections of faricimab on best-corrected visual acuity (BCVA) outcomes.

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	09 October 2018
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: 94
Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Brazil: 52
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	China: 1
Country: Number of subjects enrolled	Czechia: 67
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Hong Kong: 11
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	Poland: 93
Country: Number of subjects enrolled	Portugal: 21
Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	Singapore: 8
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Switzerland: 1

Country: Number of subjects enrolled	Taiwan: 21
Country: Number of subjects enrolled	Thailand: 14
Country: Number of subjects enrolled	Turkey: 11
Country: Number of subjects enrolled	United Kingdom: 58
Country: Number of subjects enrolled	United States: 305
Worldwide total number of subjects	951
EEA total number of subjects	271

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)	542
From 65 to 84 years	406
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1715 patients were screened, and 764 patients failed screening due to not meeting the inclusion criteria. A total of 951 patients with DME were randomized 1:1:1 using a stratified permuted-block randomization scheme into the study: 317 to Arm A: Faricimab 6 mg Q8W, 319 to Arm B: Faricimab 6 mg PTI, and 315 to Arm C: Aflibercept 2 mg Q8W.

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	A: Faricimab 6 mg Q8W

Arm description:

Participants randomized to Arm A received 6 milligrams (mg) faricimab intravitreal (IVT) injections once every 4 weeks (Q4W) to Week 20, followed by 6 mg faricimab IVT injections once every 8 weeks (Q8W) to Week 96, followed by the final study visit at Week 100.

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

Dosage and administration details:

Participants randomized to Arm A received 6 milligrams (mg) faricimab intravitreal (IVT) injections once every 4 weeks (Q4W) to Week 20, followed by 6 mg faricimab IVT injections once every 8 weeks (Q8W) to Week 96.

Arm title	B: Faricimab 6 mg PTI

Arm description:

Participants randomized to Arm B received 6 milligrams (mg) faricimab intravitreal (IVT) injections Q4W to at least Week 12, followed by a personalized treatment interval (PTI) dosing of 6 mg faricimab IVT injections up to once every 16 weeks (Q16W) through Week 96, followed by the final study visit at Week 100.

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

Dosage and administration details:

Participants randomized to Arm B received 6 milligrams (mg) faricimab intravitreal (IVT) injections Q4W to at least Week 12, followed by a personalized treatment interval (PTI) dosing of 6 mg faricimab IVT injections up to once every 16 weeks (Q16W) through Week 96.

Arm title	C: Aflibercept 2 mg Q8W

Arm description:

Participants randomized to Arm C received 2 milligrams (mg) aflibercept intravitreal (IVT) injections Q4W to Week 16, followed by 2 mg aflibercept IVT injections Q8W to Week 96, followed by the final study visit at Week 100.

Arm type	Active comparator
Investigational medicinal product name	Aflibercept
Investigational medicinal product code	
Other name	Eylea
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Participants randomized to Arm C received 2 milligrams (mg) aflibercept intravitreal (IVT) injections Q4W to Week 16, followed by 2 mg aflibercept IVT injections Q8W to Week 96.

Number of subjects in period 1	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W
Started	317	319	315
Received at Least One Dose of Study Drug	317	319	314
Completed up to Week 56	298	312	299
Completed	275	288	267
Not completed	42	31	48
Consent withdrawn by subject	11	9	13
Physician decision	2	1	6
Adverse event, non-fatal	4	5	6
Death	12	9	10
Not Specified	2	2	3
Pregnancy	-	-	1
Lost to follow-up	11	5	8
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	A: Faricimab 6 mg Q8W
Reporting group description:	
Participants randomized to Arm A received 6 milligrams (mg) faricimab intravitreal (IVT) injections once every 4 weeks (Q4W) to Week 20, followed by 6 mg faricimab IVT injections once every 8 weeks (Q8W) to Week 96, followed by the final study visit at Week 100.	
Reporting group title	B: Faricimab 6 mg PTI
Reporting group description:	
Participants randomized to Arm B received 6 milligrams (mg) faricimab intravitreal (IVT) injections Q4W to at least Week 12, followed by a personalized treatment interval (PTI) dosing of 6 mg faricimab IVT injections up to once every 16 weeks (Q16W) through Week 96, followed by the final study visit at Week 100.	
Reporting group title	C: Aflibercept 2 mg Q8W
Reporting group description:	
Participants randomized to Arm C received 2 milligrams (mg) aflibercept intravitreal (IVT) injections Q4W to Week 16, followed by 2 mg aflibercept IVT injections Q8W to Week 96, followed by the final study visit at Week 100.	

Reporting group values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W
Number of subjects	317	319	315
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)	176	183	183
From 65-84 years	140	135	131
85 years and over	1	1	1
Age Continuous			
Units: Years			
arithmetic mean	62.5	61.6	62.3
standard deviation	± 10.1	± 10.1	± 10.1
Sex: Female, Male			
Units: Participants			
Female	123	120	129
Male	194	199	186
Number of Participants by Previous Treatment Status with Intravitreal Anti-VEGF Agents			
The Treatment-Naive Population was defined as all participants randomized in the study who had not received any intravitreal (IVT) anti-VEGF agents in the study eye prior to randomization.			
Units: Subjects			
Treatment-Naive	254	255	248
Previously Treated	63	64	67
Race (NIH/OMB)			

Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	34	36	32
Native Hawaiian or Other Pacific Islander	2	0	0
Black or African American	18	23	24
White	250	249	253
More than one race	2	1	0
Unknown or Not Reported	11	10	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	56	78	67
Not Hispanic or Latino	252	232	240
Unknown or Not Reported	9	9	8
Region of Enrollment Units: Subjects			
United States and Canada	110	111	109
Asia	29	29	26
Rest of the World	178	179	180
Number of Participants by the Eye Chosen as the Study Eye (Left or Right) Units: Subjects			
Left Eye	156	168	146
Right Eye	161	151	169
Number of Participants by the Baseline BCVA Letter Score Categories in the Study Eye			
Best corrected visual acuity (BCVA) was measured at a starting test distance of 4 meters using a set of three Precision VisionTM or Lighthouse distance acuity charts (modified ETDRS Charts 1, 2, and R). The BCVA letter score ranges from 0 to 100 (best score attainable), with a higher score indicating better visual acuity.			
Units: Subjects			
≤38 Letters	14	11	9
39 to 63 Letters	128	132	132
≥64 Letters	174	174	174
Missing/Invalid BCVA	1	2	0
Number of Participants by Baseline Diabetic Retinopathy Severity (DRS) Status in the Study Eye			
The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by the central reading center.			
Units: Subjects			
1 - Diabetic Retinopathy (DR) Absent	2	4	1
2 - DR Questionable / Microaneurysms Only	3	10	6
3 - Mild Non-Proliferative DR (NPDR)	90	92	94
4 - Moderate NPDR	88	72	79
5 - Moderately Severe NPDR	59	63	54
6 - Severe NPDR	50	36	51
7 - Mild Proliferative Diabetic Retinopathy (PDR)	12	26	11
8 - Moderate PDR	6	10	6

9 - High Risk PDR (DRS Level 71)	2	1	3
10 - High Risk PDR (DRS Level 75)	0	0	0
11 - Advanced PDR (DRS Level 81)	0	0	0
12 - Advanced PDR (DRS Level 85)	0	0	0
Cannot Grade	2	5	5
Missing	3	0	5
Baseline Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye			
Best corrected visual acuity (BCVA) was measured at a starting test distance of 4 meters using a set of three Precision VisionTM or Lighthouse distance acuity charts (modified ETDRS Charts 1, 2, and R). The BCVA letter score ranges from 0 to 100 (best score attainable), with a higher score indicating better visual acuity.			
Units: ETDRS Letters			
arithmetic mean	61.9	62.5	62.1
standard deviation	± 10.1	± 9.3	± 9.4
Baseline Central Subfield Thickness in the Study Eye			
Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by the central reading center.			
Units: microns			
arithmetic mean	466.2	471.3	477.3
standard deviation	± 119.4	± 127.0	± 129.4

Reporting group values	Total		
Number of subjects	951		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	542		
From 65-84 years	406		
85 years and over	3		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	372		
Male	579		
Number of Participants by Previous Treatment Status with Intravitreal Anti-VEGF Agents			
The Treatment-Naive Population was defined as all participants randomized in the study who had not received any intravitreal (IVT) anti-VEGF agents in the study eye prior to randomization.			
Units: Subjects			
Treatment-Naive	757		
Previously Treated	194		
Race (NIH/OMB)			

Units: Subjects			
American Indian or Alaska Native	1		
Asian	102		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	65		
White	752		
More than one race	3		
Unknown or Not Reported	26		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	201		
Not Hispanic or Latino	724		
Unknown or Not Reported	26		
Region of Enrollment Units: Subjects			
United States and Canada	330		
Asia	84		
Rest of the World	537		
Number of Participants by the Eye Chosen as the Study Eye (Left or Right) Units: Subjects			
Left Eye	470		
Right Eye	481		
Number of Participants by the Baseline BCVA Letter Score Categories in the Study Eye			
Best corrected visual acuity (BCVA) was measured at a starting test distance of 4 meters using a set of three Precision VisionTM or Lighthouse distance acuity charts (modified ETDRS Charts 1, 2, and R). The BCVA letter score ranges from 0 to 100 (best score attainable), with a higher score indicating better visual acuity.			
Units: Subjects			
≤38 Letters	34		
39 to 63 Letters	392		
≥64 Letters	522		
Missing/Invalid BCVA	3		
Number of Participants by Baseline Diabetic Retinopathy Severity (DRS) Status in the Study Eye			
The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by the central reading center.			
Units: Subjects			
1 - Diabetic Retinopathy (DR) Absent	7		
2 - DR Questionable / Microaneurysms Only	19		
3 - Mild Non-Proliferative DR (NPDR)	276		
4 - Moderate NPDR	239		
5 - Moderately Severe NPDR	176		
6 - Severe NPDR	137		
7 - Mild Proliferative Diabetic Retinopathy (PDR)	49		
8 - Moderate PDR	22		

9 - High Risk PDR (DRS Level 71)	6		
10 - High Risk PDR (DRS Level 75)	0		
11 - Advanced PDR (DRS Level 81)	0		
12 - Advanced PDR (DRS Level 85)	0		
Cannot Grade	12		
Missing	8		
Baseline Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye			
Best corrected visual acuity (BCVA) was measured at a starting test distance of 4 meters using a set of three Precision VisionTM or Lighthouse distance acuity charts (modified ETDRS Charts 1, 2, and R). The BCVA letter score ranges from 0 to 100 (best score attainable), with a higher score indicating better visual acuity.			
Units: ETDRS Letters			
arithmetic mean			
standard deviation	-		
Baseline Central Subfield Thickness in the Study Eye			
Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by the central reading center.			
Units: microns			
arithmetic mean			
standard deviation	-		

Subject analysis sets

Subject analysis set title	A: Faricimab 6 mg Q8W, TN Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The treatment-naive (TN) population was defined as all patients randomized in the study who had not received any intravitreal anti-VEGF agents in the study eye prior to randomization. Participants randomized to Arm A received 6 milligrams (mg) faricimab intravitreal (IVT) injections once every 4 weeks (Q4W) to Week 20, followed by 6 mg faricimab IVT injections once every 8 weeks (Q8W) to Week 96, followed by the final study visit at Week 100.

Subject analysis set title	B: Faricimab 6 mg PTI, TN Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The treatment-naive (TN) population was defined as all patients randomized in the study who had not received any intravitreal anti-VEGF agents in the study eye prior to randomization. Participants randomized to Arm B received 6 milligrams (mg) faricimab intravitreal (IVT) injections Q4W to at least Week 12, followed by a personalized treatment interval (PTI) dosing of 6 mg faricimab IVT injections up to once every 16 weeks (Q16W) through Week 96, followed by the final study visit at Week 100.

Subject analysis set title	C: Aflibercept 2 mg Q8W, TN Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The treatment-naive (TN) population was defined as all patients randomized in the study who had not received any intravitreal anti-VEGF agents in the study eye prior to randomization. Participants randomized to Arm C received 2 milligrams (mg) aflibercept intravitreal (IVT) injections Q4W to Week 16, followed by 2 mg aflibercept IVT injections Q8W to Week 96, followed by the final study visit at Week 100.

Reporting group values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population
Number of subjects	254	255	248
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	62.5	61.3	62.5
standard deviation	± 9.9	± 10.3	± 10.0
Sex: Female, Male Units: Participants			
Female	100	94	97
Male	154	161	151
Number of Participants by Previous Treatment Status with Intravitreal Anti-VEGF Agents			
The Treatment-Naive Population was defined as all participants randomized in the study who had not received any intravitreal (IVT) anti-VEGF agents in the study eye prior to randomization.			
Units: Subjects			
Treatment-Naive Previously Treated			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	26	29	25
Native Hawaiian or Other Pacific Islander	2	0	0
Black or African American	16	20	17
White	197	197	201
More than one race	2	1	0
Unknown or Not Reported	11	8	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	42	57	54
Not Hispanic or Latino	204	190	188
Unknown or Not Reported	8	8	6
Region of Enrollment Units: Subjects			
United States and Canada	87	88	84
Asia	23	24	21
Rest of the World	144	143	143
Number of Participants by the Eye Chosen as the Study Eye (Left or Right) Units: Subjects			
Left Eye	128	136	117
Right Eye	126	119	131
Number of Participants by the Baseline BCVA Letter Score Categories in the Study Eye			
Best corrected visual acuity (BCVA) was measured at a starting test distance of 4 meters using a set of three Precision VisionTM or Lighthouse distance acuity charts (modified ETDRS Charts 1, 2, and R). The			

BCVA letter score ranges from 0 to 100 (best score attainable), with a higher score indicating better visual acuity.			
Units: Subjects			
≤38 Letters	10	8	5
39 to 63 Letters	100	103	100
≥64 Letters	143	142	143
Missing/Invalid BCVA	1	2	0
Number of Participants by Baseline Diabetic Retinopathy Severity (DRS) Status in the Study Eye			
The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by the central reading center.			
Units: Subjects			
1 - Diabetic Retinopathy (DR) Absent	2	3	1
2 - DR Questionable / Microaneurysms Only	1	8	6
3 - Mild Non-Proliferative DR (NPDR)	63	66	71
4 - Moderate NPDR	74	59	56
5 - Moderately Severe NPDR	48	56	43
6 - Severe NPDR	44	32	47
7 - Mild Proliferative Diabetic Retinopathy (PDR)	11	17	7
8 - Moderate PDR	5	9	5
9 - High Risk PDR (DRS Level 71)	2	1	3
10 - High Risk PDR (DRS Level 75)	0	0	0
11 - Advanced PDR (DRS Level 81)	0	0	0
12 - Advanced PDR (DRS Level 85)	0	0	0
Cannot Grade	1	4	4
Missing	3	0	5
Baseline Best Corrected Visual Acuity (BCVA) Letter Score in the Study Eye			
Best corrected visual acuity (BCVA) was measured at a starting test distance of 4 meters using a set of three Precision VisionTM or Lighthouse distance acuity charts (modified ETDRS Charts 1, 2, and R). The BCVA letter score ranges from 0 to 100 (best score attainable), with a higher score indicating better visual acuity.			
Units: ETDRS Letters			
arithmetic mean	62.1	62.8	62.6
standard deviation	± 10.1	± 9.3	± 9.2
Baseline Central Subfield Thickness in the Study Eye			
Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by the central reading center.			
Units: microns			
arithmetic mean	464.6	473.0	474.3
standard deviation	± 117.9	± 130.5	± 129.5

End points reporting groups

Reporting group title	A: Faricimab 6 mg Q8W

Reporting group description:

Participants randomized to Arm A received 6 milligrams (mg) faricimab intravitreal (IVT) injections once every 4 weeks (Q4W) to Week 20, followed by 6 mg faricimab IVT injections once every 8 weeks (Q8W) to Week 96, followed by the final study visit at Week 100.

Reporting group title	B: Faricimab 6 mg PTI

Reporting group description:

Participants randomized to Arm B received 6 milligrams (mg) faricimab intravitreal (IVT) injections Q4W to at least Week 12, followed by a personalized treatment interval (PTI) dosing of 6 mg faricimab IVT injections up to once every 16 weeks (Q16W) through Week 96, followed by the final study visit at Week 100.

Reporting group title	C: Aflibercept 2 mg Q8W

Reporting group description:

Participants randomized to Arm C received 2 milligrams (mg) aflibercept intravitreal (IVT) injections Q4W to Week 16, followed by 2 mg aflibercept IVT injections Q8W to Week 96, followed by the final study visit at Week 100.

Subject analysis set title	A: Faricimab 6 mg Q8W, TN Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The treatment-naive (TN) population was defined as all patients randomized in the study who had not received any intravitreal anti-VEGF agents in the study eye prior to randomization. Participants randomized to Arm A received 6 milligrams (mg) faricimab intravitreal (IVT) injections once every 4 weeks (Q4W) to Week 20, followed by 6 mg faricimab IVT injections once every 8 weeks (Q8W) to Week 96, followed by the final study visit at Week 100.

Subject analysis set title	B: Faricimab 6 mg PTI, TN Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The treatment-naive (TN) population was defined as all patients randomized in the study who had not received any intravitreal anti-VEGF agents in the study eye prior to randomization. Participants randomized to Arm B received 6 milligrams (mg) faricimab intravitreal (IVT) injections Q4W to at least Week 12, followed by a personalized treatment interval (PTI) dosing of 6 mg faricimab IVT injections up to once every 16 weeks (Q16W) through Week 96, followed by the final study visit at Week 100.

Subject analysis set title	C: Aflibercept 2 mg Q8W, TN Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The treatment-naive (TN) population was defined as all patients randomized in the study who had not received any intravitreal anti-VEGF agents in the study eye prior to randomization. Participants randomized to Arm C received 2 milligrams (mg) aflibercept intravitreal (IVT) injections Q4W to Week 16, followed by 2 mg aflibercept IVT injections Q8W to Week 96, followed by the final study visit at Week 100.

Primary: Change From Baseline in BCVA in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point title	Change From Baseline in BCVA in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. For the Mixed Model for Repeated Measures (MMRM) analysis, the model adjusted for treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), baseline BCVA (<64 vs. ≥64 letters), prior intravitreal anti-VEGF therapy (yes vs. no), and region of enrollment. An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. Invalid BCVA values were excluded. 97.5% CI is a rounding of 97.52% CI.

End point type	Primary
End point timeframe:	
From Baseline through Week 56	

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	317	319	315	254
Units: ETDRS Letters				
arithmetic mean (confidence interval 97.5%)	11.8 (10.6 to 13.0)	10.8 (9.6 to 11.9)	10.3 (9.1 to 11.4)	11.7 (10.4 to 13.0)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	255	248		
Units: ETDRS Letters				
arithmetic mean (confidence interval 97.5%)	11.2 (9.9 to 12.4)	10.5 (9.2 to 11.9)		

Statistical analyses

Statistical analysis title	Non-Inferiority: Arm A vs. Arm C, ITT

Statistical analysis description:

Three hypotheses were tested in order for each faricimab arm (Q8W or PTI) separately against the aflibercept arm using a graph-based testing procedure. The analysis presented here is for the non-inferiority of Arm A: Faricimab 6 mg Q8W compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	632
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Adjusted mean difference
Point estimate	1.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.1
upper limit	3.2
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[1] - If the lower bound of the two-sided 97.52% confidence interval for the difference in adjusted means for the faricimab 6 mg Q8W and the active comparator (aflibercept 2 mg Q8W) arms was greater than –4 letters, then faricimab 6 mg Q8W was considered non-inferior to aflibercept 2 mg Q8W. Non-inferiority was tested one-sided at a significance level of α = 0.0248.

Statistical analysis title	Non-Inferiority: Arm B vs. Arm C, ITT

Statistical analysis description:

Three hypotheses were tested in order for each faricimab arm (Q8W or PTI) separately against the aflibercept arm using a graph-based testing procedure. The analysis presented here is for the non-inferiority of Arm B: Faricimab 6 mg PTI compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	634
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Adjusted mean difference
Point estimate	0.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.1
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[2] - If the lower bound of the two-sided 97.52% confidence interval for the difference in adjusted means for the faricimab 6 mg PTI and the active comparator (aflibercept 2 mg Q8W) arms was greater than –4 letters, then faricimab 6 mg PTI was considered non-inferior to aflibercept 2 mg Q8W. Non-inferiority was tested one-sided at a significance level of α = 0.0248.

Statistical analysis title	Superiority: Arm A vs. Arm C, TN

Statistical analysis description:

Three hypotheses were tested in order for each faricimab arm (Q8W or PTI) separately against the aflibercept arm using a graph-based testing procedure. The analysis presented here is for the superiority of Arm A: Faricimab 6 mg Q8W compared with Arm C: Aflibercept 2 mg Q8W in the Treatment-Naive Population.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	502
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1718 [3]
Method	Mixed Model for Repeated Measures
Parameter estimate	Adjusted mean difference
Point estimate	1.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.7
upper limit	3
Variability estimate	Standard error of the mean
Dispersion value	0.83

Notes:

[3] - Tested at an overall significance level of α = 0.0248.

Statistical analysis title	Superiority: Arm B vs. Arm C, TN

Statistical analysis description:

Three hypotheses were tested in order for each faricimab arm (Q8W or PTI) separately against the aflibercept arm using a graph-based testing procedure. The analysis presented here is for the superiority of Arm B: Faricimab 6 mg PTI compared with Arm C: Aflibercept 2 mg Q8W in the Treatment-Naive Population.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4602 [4]
Method	Mixed Model for Repeated Measures
Parameter estimate	Adjusted mean difference
Point estimate	0.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.2
upper limit	2.4
Variability estimate	Standard error of the mean
Dispersion value	0.82

Notes:

[4] - Tested at an overall significance level of α = 0.0248.

Statistical analysis title	Superiority: Arm A vs. Arm C, ITT

Statistical analysis description:

Three hypotheses were tested in order for each faricimab arm (Q8W or PTI) separately against the aflibercept arm using a graph-based testing procedure. The analysis presented here is for the superiority of Arm A: Faricimab 6 mg Q8W compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	632
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0361 [5]
Method	Mixed Model for Repeated Measures
Parameter estimate	Adjusted mean difference
Point estimate	1.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.1
upper limit	3.2
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[5] - Tested at an overall significance level of α = 0.0248.

Statistical analysis title	Superiority: Arm B vs. Arm C, ITT

Statistical analysis description:

Three hypotheses were tested in order for each faricimab arm (Q8W or PTI) separately against the aflibercept arm using a graph-based testing procedure. The analysis presented here is for the superiority

of Arm B: Faricimab 6 mg PTI compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	634
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.493 [6]
Method	Mixed Model for Repeated Measures
Parameter estimate	Adjusted mean difference
Point estimate	0.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.1
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	0.73

Notes:

[6] - Tested at an overall significance level of α = 0.0248.

Secondary: Percentage of Participants with a ≥2-Step Diabetic Retinopathy Severity (DRS) Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale (DRSS) at Week 52, ITT and Treatment-Naive Populations

End point title	Percentage of Participants with a ≥2-Step Diabetic Retinopathy Severity (DRS) Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale (DRSS) at Week 52, ITT and Treatment-Naive Populations

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 97.5% confidence interval (CI) is a rounding of 97.52% CI.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	231	251	238	179
Units: Percentage of participants				
number (confidence interval 97.5%)	44.2 (37.1 to 51.4)	43.7 (36.8 to 50.7)	46.8 (39.8 to 53.8)	46.9 (38.7 to 55.1)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	198	184		
Units: Percentage of participants				
number (confidence interval 97.5%)	45.7 (37.8 to 53.7)	52.3 (44.2 to 60.4)		

Statistical analyses

Statistical analysis title	Non-Inferiority: Arm A vs. Arm C, ITT

Statistical analysis description:

This analysis is for the non-inferiority of Arm A: Faricimab 6 mg Q8W compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-2.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-12.6
upper limit	7.4

Notes:

[7] - If the lower bound of the two-sided 97.52% confidence interval for the difference in CMH weighted percentages of participants for the faricimab Q8W and the active comparator (aflibercept Q8W) arms was greater than –10%, then faricimab Q8W was considered non-inferior to aflibercept.

Statistical analysis title	Non-Inferiority: Arm B vs. Arm C, ITT

Statistical analysis description:

This analysis is for the non-inferiority of Arm B: Faricimab 6 mg PTI compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-3.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-13.4
upper limit	6.3

Notes:

[8] - If the lower bound of the two-sided 97.52% confidence interval for the difference in CMH weighted percentages of participants for the faricimab PTI and the active comparator (aflibercept Q8W) arms was greater than –10%, then faricimab PTI was considered non-inferior to aflibercept.

Statistical analysis title	Superiority: Arm A vs. Arm C, TN

Statistical analysis description:

This analysis is for the superiority of Arm A: Faricimab 6 mg Q8W compared with Arm C: Aflibercept 2 mg Q8W in the Treatment-Naive Population.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	363
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3009 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-5.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-16.9
upper limit	6.1

Notes:

[9] - Tested at an overall significance level of α = 0.0248.

Statistical analysis title	Superiority: Arm B vs. Arm C, TN

Statistical analysis description:

This analysis is for the superiority of Arm B: Faricimab 6 mg PTI compared with Arm C: Aflibercept 2 mg Q8W in the Treatment-Naive Population.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	382
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1735 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-6.9
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-18.3
upper limit	4.4

Notes:

[10] - Tested at an overall significance level of α = 0.0248.

Statistical analysis title	Superiority: Arm A vs. Arm C, ITT

Statistical analysis description:

This analysis is for the superiority of Arm A: Faricimab 6 mg Q8W compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W

Number of subjects included in analysis	469
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5757 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-2.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-12.6
upper limit	7.4

Notes:

[11] - Tested at an overall significance level of α = 0.0248.

Statistical analysis title	Superiority: Arm B vs. Arm C, ITT

Statistical analysis description:

This analysis is for the superiority of Arm B: Faricimab 6 mg PTI compared with Arm C: Aflibercept 2 mg Q8W in the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4293 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-3.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-13.4
upper limit	6.3

Notes:

[12] - Tested at an overall significance level of α = 0.0248.

Secondary: Change from Baseline in BCVA in the Study Eye Over Time, ITT Population

End point title	Change from Baseline in BCVA in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. For the Mixed Model for Repeated Measures (MMRM) analysis, the model adjusted for treatment arm, visit, visit-by-treatment arm interaction, baseline BCVA (continuous), baseline BCVA (<64 vs. ≥64 letters), prior intravitreal anti-VEGF therapy (yes vs. no), and region of enrollment. An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. Invalid BCVA values were excluded. 95% CI is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 4	6.1 (5.4 to 6.8)	6.6 (5.8 to 7.3)	6.4 (5.7 to 7.1)	
Week 8	7.8 (7.0 to 8.5)	8.1 (7.4 to 8.9)	7.5 (6.8 to 8.3)	
Week 12	8.7 (7.8 to 9.5)	9.1 (8.2 to 9.9)	8.5 (7.7 to 9.4)	
Week 16	9.9 (9.0 to 10.7)	9.8 (9.0 to 10.7)	8.8 (7.9 to 9.6)	
Week 20	10.1 (9.2 to 10.9)	9.5 (8.6 to 10.4)	8.8 (8.0 to 9.7)	
Week 24	10.6 (9.7 to 11.5)	9.9 (9.0 to 10.8)	9.3 (8.4 to 10.2)	
Week 28	10.7 (9.7 to 11.6)	10.5 (9.6 to 11.4)	9.6 (8.7 to 10.5)	
Week 32	11.3 (10.3 to 12.3)	10.2 (9.2 to 11.1)	9.4 (8.5 to 10.4)	
Week 36	11.0 (10.1 to 12.0)	10.6 (9.6 to 11.6)	10.4 (9.5 to 11.4)	
Week 40	11.4 (10.3 to 12.5)	10.7 (9.6 to 11.7)	10.3 (9.2 to 11.3)	
Week 44	11.7 (10.7 to 12.7)	10.9 (9.9 to 11.9)	10.5 (9.5 to 11.5)	
Week 48	11.8 (10.7 to 12.9)	10.6 (9.5 to 11.7)	10.1 (9.0 to 11.1)	
Week 52	11.6 (10.5 to 12.6)	10.7 (9.6 to 11.7)	10.4 (9.3 to 11.4)	
Week 56	11.6 (10.4 to 12.8)	10.6 (9.5 to 11.8)	9.9 (8.7 to 11.1)	
Week 60	11.4 (10.2 to 12.6)	10.1 (8.9 to 11.3)	10.1 (8.9 to 11.3)	
Week 64	11.6 (10.4 to 12.7)	10.3 (9.2 to 11.5)	9.4 (8.2 to 10.6)	
Week 68	11.2 (10.0 to 12.3)	10.1 (9.0 to 11.3)	10.0 (8.8 to 11.1)	
Week 72	11.2 (9.9 to 12.4)	9.9 (8.8 to 11.1)	9.4 (8.2 to 10.6)	
Week 76	10.6 (9.3 to 11.9)	9.4 (8.1 to 10.7)	9.5 (8.2 to 10.8)	
Week 80	10.6 (9.2 to 12.0)	9.5 (8.1 to 10.9)	9.1 (7.7 to 10.5)	
Week 84	9.8 (8.4 to 11.2)	10.3 (9.0 to 11.7)	9.6 (8.2 to 11.0)	
Week 88	9.8 (8.4 to 11.3)	10.0 (8.6 to 11.4)	9.2 (7.7 to 10.6)	
Week 92	10.8 (9.3 to 12.2)	10.2 (8.8 to 11.7)	9.3 (7.9 to 10.8)	
Week 96	11.3 (9.8 to 12.8)	10.5 (9.1 to 12.0)	9.0 (7.5 to 10.5)	
Week 100	10.7 (9.1 to 12.3)	9.5 (7.9 to 11.0)	9.8 (8.2 to 11.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in BCVA in the Study Eye Over Time, Treatment-Naive Population

End point title	Change from Baseline in BCVA in the Study Eye Over Time, Treatment-Naive Population

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 attainable), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. For the Mixed Model for Repeated Measures (MMRM) analysis, the model adjusted for treatment group, visit, visit-by-treatment group interaction, baseline BCVA (continuous), baseline BCVA (<64 vs. ≥64 letters), and region of enrollment. An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[13]	248	
Units: ETDRS Letters				
arithmetic mean (confidence interval 95%)				
Week 4	6.0 (5.2 to 6.9)	6.7 (5.8 to 7.5)	6.3 (5.4 to 7.1)	
Week 8	7.5 (6.6 to 8.4)	8.2 (7.3 to 9.1)	7.3 (6.4 to 8.2)	
Week 12	8.7 (7.8 to 9.6)	9.2 (8.3 to 10.1)	8.5 (7.6 to 9.5)	
Week 16	9.7 (8.8 to 10.7)	10.0 (9.1 to 10.9)	8.7 (7.8 to 9.6)	
Week 20	10.0 (9.1 to 11.0)	9.8 (8.8 to 10.7)	9.0 (8.1 to 10.0)	
Week 24	10.6 (9.6 to 11.6)	10.2 (9.2 to 11.2)	9.4 (8.4 to 10.4)	
Week 28	10.8 (9.8 to 11.8)	10.8 (9.8 to 11.8)	9.9 (8.9 to 10.9)	
Week 32	11.2 (10.1 to 12.3)	10.3 (9.2 to 11.4)	9.9 (8.8 to 11.0)	
Week 36	10.8 (9.7 to 11.9)	10.9 (9.8 to 12.0)	10.5 (9.3 to 11.6)	

Week 40	11.3 (10.2 to 12.5)	11.2 (10.0 to 12.3)	10.6 (9.5 to 11.8)	
Week 44	11.5 (10.4 to 12.7)	11.2 (10.1 to 12.3)	11.1 (9.9 to 12.2)	
Week 48	11.4 (10.2 to 12.7)	10.9 (9.7 to 12.1)	10.5 (9.3 to 11.7)	
Week 52	11.7 (10.5 to 12.8)	11.1 (9.9 to 12.2)	10.7 (9.5 to 11.9)	
Week 56	11.4 (10.0 to 12.8)	11.0 (9.6 to 12.3)	10.0 (8.6 to 11.4)	
Week 60	11.4 (10.0 to 12.7)	10.5 (9.2 to 11.8)	10.1 (8.8 to 11.5)	
Week 64	11.6 (10.2 to 12.9)	10.5 (9.2 to 11.8)	9.5 (8.2 to 10.8)	
Week 68	11.2 (9.9 to 12.5)	10.3 (9.0 to 11.6)	10.0 (8.7 to 11.3)	
Week 72	11.1 (9.7 to 12.5)	10.1 (8.8 to 11.5)	9.6 (8.2 to 10.9)	
Week 76	10.6 (9.0 to 12.1)	9.7 (8.2 to 11.2)	9.5 (8.0 to 11.1)	
Week 80	10.9 (9.4 to 12.5)	10.0 (8.5 to 11.5)	9.3 (7.8 to 10.9)	
Week 84	9.9 (8.4 to 11.5)	10.8 (9.3 to 12.3)	9.6 (8.0 to 11.1)	
Week 88	9.6 (7.9 to 11.2)	10.2 (8.6 to 11.8)	9.4 (7.8 to 11.1)	
Week 92	10.4 (8.8 to 12.1)	10.6 (9.0 to 12.2)	9.6 (7.9 to 11.2)	
Week 96	10.6 (8.9 to 12.3)	10.9 (9.2 to 12.5)	9.0 (7.3 to 10.7)	
Week 100	10.4 (8.5 to 12.2)	10.0 (8.2 to 11.7)	9.8 (7.9 to 11.6)	

Notes:

[13] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining Greater Than or Equal to (≥)15, ≥10, ≥5, or ≥0 Letters in BCVA from Baseline in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT Population

End point title	Percentage of Participants Gaining Greater Than or Equal to (≥)15, ≥10, ≥5, or ≥0 Letters in BCVA from Baseline in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	268	293	279	
Units: Percentage of participants				
number (confidence interval 95%)				
Gaining ≥15 Letters	33.8 (28.4 to 39.2)	28.5 (23.6 to 33.3)	30.3 (25.0 to 35.5)	
Gaining ≥10 Letters	59.3 (53.6 to 64.9)	53.0 (47.5 to 58.5)	53.9 (48.3 to 59.5)	
Gaining ≥5 Letters	81.8 (77.3 to 86.4)	77.4 (72.7 to 82.1)	78.0 (73.3 to 82.7)	
Gaining ≥0 Letters	92.1 (89.0 to 95.3)	91.1 (87.8 to 94.3)	91.4 (88.2 to 94.6)	

Statistical analyses

Statistical analysis title	Gaining ≥15 Letters: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥15 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	11.1

Statistical analysis title	Gaining ≥15 Letters: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥15 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	5.2

Statistical analysis title	Gaining ≥10 Letters: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥10 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	13.4

Statistical analysis title	Gaining ≥10 Letters: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥10 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.9
upper limit	6.8

Statistical analysis title	Gaining ≥5 Letters: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥5 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W

Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	10.3

Statistical analysis title	Gaining ≥5 Letters: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants gaining ≥5 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	5.9

Statistical analysis title	Gaining ≥0 Letters: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants gaining ≥0 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	5.2

Statistical analysis title	Gaining ≥0 Letters: Arm B vs. Arm C

Statistical analysis description:	
This is the difference in percentage of participants gaining ≥0 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	4.2

Secondary: Percentage of Participants Gaining ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Gaining ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,306,309)	13.4 (9.9 to 17.0)	10.8 (7.5 to 14.2)	10.6 (7.3 to 14.0)	
Week 8 (n = 305,311,309)	15.2 (11.2 to 19.1)	16.7 (12.7 to 20.8)	15.4 (11.5 to 19.4)	
Week 12 (n = 305,303,302)	20.7 (16.3 to 25.1)	22.1 (17.6 to 26.5)	19.3 (15.0 to 23.6)	
Week 16 (n = 300,304,296)	24.4 (19.7 to 29.1)	24.3 (19.7 to 28.8)	23.1 (18.5 to 27.7)	
Week 20 (n = 294,302,295)	26.7 (21.8 to 31.6)	21.3 (16.8 to 25.7)	22.8 (18.3 to 27.4)	

Week 24 (n = 293,306,297)	29.8 (24.7 to 34.9)	24.0 (19.3 to 28.6)	24.6 (19.8 to 29.3)	
Week 28 (n = 284,295,287)	30.1 (25.0 to 35.3)	26.7 (21.9 to 31.5)	25.7 (20.7 to 30.6)	
Week 32 (n = 277,284,280)	35.9 (30.6 to 41.3)	27.3 (22.2 to 32.3)	23.9 (19.1 to 28.7)	
Week 36 (n = 275,281,275)	33.8 (28.5 to 39.1)	32.1 (27.0 to 37.2)	28.5 (23.5 to 33.5)	
Week 40 (n = 275,286,274)	37.8 (32.3 to 43.3)	30.5 (25.4 to 35.6)	29.1 (24.0 to 34.2)	
Week 44 (n = 269,286,272)	37.1 (31.6 to 42.5)	30.1 (25.0 to 32.5)	33.4 (28.0 to 38.7)	
Week 48 (n = 255,286,278)	33.0 (27.5 to 38.6)	29.4 (24.4 to 34.3)	29.3 (24.1 to 34.4)	
Week 52 (n = 267,281,271)	35.0 (29.6 to 40.4)	31.0 (25.9 to 36.2)	33.1 (27.7 to 38.5)	
Week 56 (n = 267,283,261)	38.8 (33.2 to 44.3)	29.5 (24.5 to 34.6)	36.4 (30.7 to 42.0)	
Week 60 (n = 261,277,255)	38.0 (32.3 to 43.7)	30.3 (25.2 to 35.5)	36.6 (30.9 to 42.3)	
Week 64 (n = 258,290,259)	40.3 (34.7 to 45.9)	29.6 (24.5 to 34.8)	31.9 (26.5 to 37.3)	
Week 68 (n = 254,272,255)	36.9 (31.3 to 42.5)	31.1 (25.8 to 36.5)	35.4 (29.8 to 41.0)	
Week 72 (n = 245,261,250)	36.8 (31.0 to 42.6)	30.5 (25.1 to 35.8)	32.5 (26.9 to 38.0)	
Week 76 (n = 257,273,251)	37.1 (31.5 to 42.7)	31.2 (25.9 to 36.6)	35.1 (29.4 to 40.8)	
Week 80 (n = 247,269,250)	39.6 (33.8 to 45.5)	30.1 (24.8 to 35.3)	35.3 (29.6 to 41.1)	
Week 84 (n = 253,265,255)	38.5 (32.9 to 44.2)	30.6 (25.2 to 36.0)	38.1 (32.4 to 43.9)	
Week 88 (n = 254,267,247)	40.4 (34.7 to 46.1)	29.6 (24.3 to 35.0)	38.5 (32.6 to 44.3)	
Week 92 (n = 249,269,242)	42.3 (36.4 to 48.1)	34.6 (29.2 to 40.0)	42.1 (36.0 to 48.2)	
Week 96 (n = 244,267,241)	44.2 (38.1 to 50.2)	34.4 (29.0 to 39.7)	36.0 (30.1 to 41.8)	
Week 100 (n = 251,271,237)	43.1 (37.1 to 49.1)	31.2 (25.9 to 36.5)	40.8 (34.8 to 46.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Gaining ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related

intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,306,309)	29.1 (24.2 to 34.0)	26.9 (22.1 to 31.8)	28.7 (23.8 to 33.6)	
Week 8 (n = 305,311,309)	39.7 (34.4 to 45.1)	41.4 (36.0 to 46.9)	34.8 (29.6 to 40.0)	
Week 12 (n = 305,303,302)	44.8 (39.3 to 50.2)	46.9 (41.4 to 52.4)	43.2 (37.7 to 48.8)	
Week 16 (n = 300,304,296)	52.5 (46.9 to 58.0)	51.3 (45.9 to 56.7)	41.8 (36.3 to 47.3)	
Week 20 (n = 294,302,295)	54.0 (48.6 to 59.5)	50.0 (44.5 to 55.6)	45.5 (40.0 to 51.0)	
Week 24 (n = 293,306,297)	57.0 (51.5 to 62.5)	52.8 (47.4 to 58.3)	48.4 (42.9 to 53.9)	
Week 28 (n = 284,295,287)	58.3 (52.7 to 63.9)	51.3 (45.8 to 56.8)	51.7 (46.1 to 57.3)	
Week 32 (n = 277,284,280)	60.1 (54.4 to 65.8)	50.9 (45.2 to 56.6)	52.5 (46.8 to 58.1)	
Week 36 (n = 275,281,275)	58.6 (52.9 to 64.2)	57.3 (51.7 to 62.9)	58.7 (53.0 to 64.3)	
Week 40 (n = 275,286,274)	61.8 (56.2 to 67.4)	56.0 (50.5 to 61.6)	55.8 (50.2 to 61.4)	
Week 44 (n = 269,286,272)	62.0 (56.3 to 67.6)	55.9 (50.3 to 61.5)	57.2 (51.6 to 62.8)	
Week 48 (n = 255,286,278)	58.0 (52.1 to 63.9)	56.7 (51.1 to 62.2)	56.3 (50.7 to 61.9)	
Week 52 (n = 267,281,271)	61.1 (55.4 to 66.8)	58.7 (53.1 to 64.3)	57.1 (51.4 to 62.8)	
Week 56 (n = 267,283,261)	60.7 (55.1 to 66.4)	55.9 (50.3 to 61.5)	56.2 (50.4 to 62.0)	
Week 60 (n = 261,277,255)	58.5 (52.7 to 64.4)	53.7 (48.1 to 59.4)	57.0 (51.0 to 63.0)	
Week 64 (n = 258,290,259)	59.7 (53.8 to 65.5)	54.5 (48.9 to 60.1)	51.5 (45.6 to 57.4)	
Week 68 (n = 254,272,255)	60.2 (54.5 to 66.0)	54.1 (48.3 to 60.0)	60.7 (54.8 to 66.5)	
Week 72 (n = 245,261,250)	59.2 (53.1 to 62.5)	55.6 (49.8 to 61.4)	56.6 (50.7 to 62.5)	
Week 76 (n = 257,273,251)	58.7 (52.9 to 64.6)	52.5 (46.7 to 58.3)	57.0 (51.0 to 62.9)	
Week 80 (n = 247,269,250)	59.6 (53.6 to 65.6)	55.0 (49.2 to 60.7)	56.5 (50.4 to 62.5)	
Week 84 (n = 253,265,255)	56.2 (50.3 to 62.1)	53.3 (47.5 to 59.1)	55.8 (49.8 to 61.8)	
Week 88 (n = 254,267,247)	58.3 (52.4 to 64.1)	53.5 (47.6 to 59.5)	57.0 (51.0 to 63.0)	

Week 92 (n = 249,269,242)	59.5 (53.6 to 65.4)	55.0 (49.2 to 60.8)	58.5 (52.5 to 64.5)	
Week 96 (n = 244,267,241)	65.4 (59.5 to 71.2)	58.0 (52.1 to 63.8)	58.8 (52.6 to 64.9)	
Week 100 (n = 251,271,237)	63.7 (58.0 to 69.3)	54.0 (48.2 to 59.9)	65.3 (59.5 to 71.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥5 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Gaining ≥5 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,306,309)	57.8 (52.3 to 63.2)	61.8 (56.4 to 67.2)	59.2 (53.7 to 64.6)	
Week 8 (n = 305,311,309)	67.0 (61.9 to 72.2)	68.8 (63.7 to 73.9)	66.0 (60.7 to 71.2)	
Week 12 (n = 305,303,302)	70.9 (65.9 to 76.0)	74.3 (69.4 to 79.2)	72.5 (67.4 to 77.5)	
Week 16 (n = 300,304,296)	75.4 (70.6 to 80.2)	74.6 (69.9 to 79.4)	69.6 (64.4 to 74.8)	
Week 20 (n = 294,302,295)	76.0 (71.2 to 80.8)	79.5 (75.1 to 84.0)	71.4 (66.3 to 76.6)	
Week 24 (n = 293,306,297)	78.3 (73.7 to 83.0)	76.3 (71.6 to 80.9)	72.2 (67.2 to 77.2)	
Week 28 (n = 284,295,287)	76.8 (72.0 to 81.7)	79.4 (74.8 to 83.9)	77.2 (72.4 to 81.9)	
Week 32 (n = 277,284,280)	80.0 (75.4 to 84.6)	78.3 (73.6 to 83.0)	75.9 (70.9 to 80.8)	

Week 36 (n = 275,281,275)	79.0 (74.2 to 83.8)	80.0 (75.4 to 84.6)	78.4 (73.7 to 83.2)	
Week 40 (n = 275,286,274)	79.5 (74.8 to 84.2)	78.0 (73.2 to 82.7)	79.8 (75.1 to 84.5)	
Week 44 (n = 269,286,272)	84.0 (79.7 to 88.3)	77.5 (72.8 to 82.3)	81.9 (77.5 to 86.3)	
Week 48 (n = 255,286,278)	81.3 (76.7 to 86.0)	81.5 (77.1 to 85.9)	77.2 (72.4 to 82.0)	
Week 52 (n = 267,281,271)	81.7 (77.1 to 86.3)	78.2 (73.5 to 83.0)	77.1 (72.2 to 82.0)	
Week 56 (n = 267,283,261)	78.6 (73.8 to 83.4)	79.2 (74.5 to 83.8)	80.3 (75.7 to 84.9)	
Week 60 (n = 261,277,255)	75.7 (70.5 to 80.8)	75.9 (71.0 to 80.9)	80.3 (75.4 to 85.1)	
Week 64 (n = 258,290,259)	77.6 (72.6 to 82.6)	77.3 (72.5 to 82.0)	72.5 (67.2 to 77.8)	
Week 68 (n = 254,272,255)	77.0 (72.0 to 82.1)	76.0 (70.9 to 81.0)	78.5 (73.5 to 83.4)	
Week 72 (n = 245,261,250)	79.5 (74.5 to 84.4)	76.7 (71.6 to 81.7)	76.1 (70.8 to 81.3)	
Week 76 (n = 257,273,251)	75.6 (70.5 to 80.8)	73.8 (68.7 to 78.9)	72.6 (67.1 to 78.0)	
Week 80 (n = 247,269,250)	74.9 (69.7 to 80.2)	75.4 (70.3 to 80.5)	77.4 (72.2 to 82.5)	
Week 84 (n = 253,265,255)	73.1 (67.7 to 78.4)	79.9 (75.2 to 84.7)	75.2 (70.0 to 80.3)	
Week 88 (n = 254,267,247)	74.2 (69.0 to 79.5)	74.3 (69.2 to 79.5)	77.5 (72.4 to 82.6)	
Week 92 (n = 249,269,242)	76.5 (71.3 to 81.7)	76.6 (71.6 to 81.6)	77.4 (72.2 to 82.6)	
Week 96 (n = 244,267,241)	80.9 (76.1 to 85.7)	76.2 (71.2 to 81.2)	76.0 (70.7 to 81.3)	
Week 100 (n = 251,271,237)	80.0 (75.1 to 84.8)	75.3 (70.3 to 80.4)	81.3 (76.3 to 86.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥0 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Gaining ≥0 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,306,309)	85.1 (81.2 to 89.0)	89.2 (85.8 to 92.7)	89.3 (85.9 to 92.8)	
Week 8 (n = 305,311,309)	90.2 (86.9 to 93.5)	91.3 (88.2 to 94.4)	90.3 (87.0 to 93.6)	
Week 12 (n = 305,303,302)	90.8 (87.6 to 94.0)	92.7 (89.8 to 95.6)	90.4 (87.1 to 93.7)	
Week 16 (n = 300,304,296)	92.4 (89.4 to 95.3)	91.1 (88.0 to 94.3)	90.9 (87.7 to 94.1)	
Week 20 (n = 294,302,295)	92.2 (89.1 to 95.3)	91.7 (88.6 to 94.8)	93.9 (91.2 to 96.6)	
Week 24 (n = 293,306,297)	91.5 (88.3 to 94.7)	91.5 (88.5 to 94.6)	91.5 (88.4 to 94.7)	
Week 28 (n = 284,295,287)	92.2 (89.1 to 95.4)	94.3 (91.7 to 96.8)	94.0 (91.4 to 96.7)	
Week 32 (n = 277,284,280)	91.4 (88.2 to 94.7)	90.9 (87.6 to 94.2)	92.8 (89.8 to 95.8)	
Week 36 (n = 275,281,275)	92.4 (89.3 to 95.5)	90.5 (87.1 to 93.8)	95.0 (92.5 to 97.5)	
Week 40 (n = 275,286,274)	92.0 (88.8 to 95.2)	92.3 (89.3 to 95.4)	93.1 (90.1 to 96.0)	
Week 44 (n = 269,286,272)	91.8 (88.5 to 95.1)	91.2 (88.0 to 94.5)	92.6 (89.6 to 95.6)	
Week 48 (n = 255,286,278)	93.7 (90.7 to 96.7)	91.0 (87.7 to 94.3)	91.4 (88.2 to 94.6)	
Week 52 (n = 267,281,271)	93.6 (90.7 to 96.5)	90.4 (86.9 to 93.8)	91.9 (88.7 to 95.1)	
Week 56 (n = 267,283,261)	92.7 (89.6 to 95.7)	91.5 (88.3 to 94.7)	90.9 (87.5 to 94.3)	
Week 60 (n = 261,277,255)	89.3 (85.6 to 93.0)	88.5 (84.9 to 92.2)	92.6 (89.5 to 95.8)	
Week 64 (n = 258,290,259)	91.3 (87.9 to 94.6)	89.7 (86.2 to 93.2)	87.4 (83.4 to 91.4)	
Week 68 (n = 254,272,255)	89.4 (85.6 to 93.2)	90.5 (87.0 to 94.0)	91.3 (87.8 to 94.7)	
Week 72 (n = 245,261,250)	89.1 (85.2 to 93.0)	90.4 (86.8 to 94.0)	88.4 (84.5 to 92.3)	
Week 76 (n = 257,273,251)	89.6 (86.0 to 93.3)	86.3 (82.3 to 90.3)	90.3 (86.7 to 94.0)	
Week 80 (n = 247,269,250)	86.6 (82.5 to 90.8)	88.5 (84.7 to 92.3)	88.6 (84.6 to 92.5)	
Week 84 (n = 253,265,255)	87.1 (83.0 to 91.2)	90.2 (86.7 to 93.7)	87.9 (83.9 to 91.9)	
Week 88 (n = 254,267,247)	84.4 (80.0 to 88.9)	89.5 (85.9 to 93.1)	88.1 (84.1 to 92.0)	
Week 92 (n = 249,269,242)	86.7 (82.5 to 90.9)	86.7 (82.6 to 90.7)	87.1 (82.9 to 91.3)	
Week 96 (n = 244,267,241)	86.5 (82.3 to 90.7)	87.0 (83.0 to 91.0)	89.1 (85.2 to 93.1)	
Week 100 (n = 251,271,237)	86.1 (81.8 to 90.3)	87.5 (83.7 to 91.4)	91.1 (87.5 to 94.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥15, ≥10, ≥5, or ≥0 Letters in BCVA from Baseline in the Study Eye Averaged Over Weeks 48, 52, and 56, Treatment-Naive Population

End point title	Percentage of Participants Gaining ≥15, ≥10, ≥5, or ≥0 Letters in BCVA from Baseline in the Study Eye Averaged Over Weeks 48, 52, and 56, Treatment-Naive Population

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	208	231	213	
Units: Percentage of participants				
number (confidence interval 95%)				
Gaining ≥15 Letters	32.9 (26.7 to 39.0)	29.4 (23.9 to 34.9)	32.7 (26.5 to 38.8)	
Gaining ≥10 Letters	58.3 (51.8 to 64.8)	55.5 (49.3 to 61.7)	56.1 (49.6 to 62.5)	
Gaining ≥5 Letters	81.8 (76.5 to 87.0)	79.6 (74.5 to 84.7)	80.6 (75.4 to 85.8)	
Gaining ≥0 Letters	93.2 (89.8 to 96.7)	92.2 (88.8 to 95.6)	92.0 (88.4 to 95.6)	

Statistical analyses

Statistical analysis title	Gaining ≥15 Letters: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants gaining ≥15 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	8.9

Statistical analysis title	Gaining ≥15 Letters: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants gaining ≥15 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	4.8

Statistical analysis title	Gaining ≥10 Letters: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants gaining ≥10 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	2.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	11.4

Statistical analysis title	Gaining ≥10 Letters: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥10 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	8.1

Statistical analysis title	Gaining ≥5 Letters: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥5 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	8.5

Statistical analysis title	Gaining ≥5 Letters: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥5 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population

Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	6.2

Statistical analysis title	Gaining ≥0 Letters: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥0 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	6.2

Statistical analysis title	Gaining ≥0 Letters: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants gaining ≥0 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	5.2

Secondary: Percentage of Participants Gaining ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Gaining ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[14]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,243,242)	13.9 (9.7 to 18.0)	10.7 (7.0 to 14.4)	10.3 (6.6 to 14.1)	
Week 8 (n = 244,246,242)	14.7 (10.3 to 19.1)	17.9 (13.2 to 22.5)	15.7 (11.2 to 20.1)	
Week 12 (n = 242,241,236)	19.9 (15.0 to 24.8)	23.2 (18.1 to 28.3)	19.7 (14.8 to 24.6)	
Week 16 (n = 241,241,230)	23.3 (18.0 to 28.5)	26.0 (20.8 to 31.2)	23.5 (18.2 to 28.7)	
Week 20 (n = 233,239,230)	25.9 (20.4 to 31.4)	22.7 (17.5 to 27.9)	22.0 (16.9 to 27.1)	
Week 24 (n = 231,242,232)	30.2 (24.4 to 35.9)	24.5 (19.2 to 29.7)	24.3 (18.9 to 29.6)	
Week 28 (n = 223,232,222)	29.8 (23.9 to 35.6)	28.3 (22.7 to 33.8)	26.5 (20.8 to 32.1)	
Week 32 (n = 216,220,216)	34.4 (28.4 to 40.5)	27.9 (22.1 to 33.6)	25.1 (19.6 to 30.7)	
Week 36 (n = 212,220,209)	34.1 (28.0 to 40.2)	34.2 (28.3 to 40.1)	28.9 (23.2 to 34.5)	
Week 40 (n = 213,222,211)	37.8 (31.4 to 44.1)	32.5 (26.6 to 38.4)	28.4 (22.6 to 34.2)	
Week 44 (n = 208,223,211)	36.1 (29.9 to 42.3)	30.4 (24.6 to 36.2)	35.0 (28.7 to 41.2)	
Week 48 (n = 199,224,212)	32.8 (26.4 to 39.2)	31.2 (25.5 to 36.9)	31.7 (25.7 to 37.8)	
Week 52 (n = 209,223,207)	34.1 (27.9 to 40.3)	32.7 (26.9 to 38.6)	33.9 (27.7 to 40.2)	
Week 56 (n = 209,224,200)	39.2 (33.0 to 45.5)	30.6 (24.8 to 36.3)	37.6 (31.1 to 44.2)	
Week 60 (n = 208,219,200)	37.4 (31.0 to 43.7)	32.5 (26.5 to 38.4)	36.2 (29.9 to 42.5)	

Week 64 (n = 205,228,203)	39.8 (33.5 to 46.1)	31.1 (25.2 to 37.0)	31.9 (25.8 to 38.0)	
Week 68 (n = 201,214,200)	36.0 (29.7 to 42.3)	33.4 (27.2 to 39.7)	36.4 (30.0 to 42.8)	
Week 72 (n = 191,205,196)	35.1 (28.5 to 41.6)	33.7 (27.5 to 39.9)	34.7 (28.2 to 41.2)	
Week 76 (n = 199,216,195)	37.2 (30.9 to 43.6)	32.5 (26.4 to 38.6)	34.5 (28.0 to 40.9)	
Week 80 (n = 189,210,193)	40.1 (33.6 to 46.6)	33.8 (27.6 to 40.0)	39.4 (32.8 to 45.9)	
Week 84 (n = 194,209,199)	40.1 (33.6 to 46.6)	32.0 (25.9 to 38.1)	39.4 (32.8 to 45.9)	
Week 88 (n = 194,211,191)	39.5 (32.9 to 46.1)	29.9 (23.8 to 35.9)	38.4 (31.8 to 45.0)	
Week 92 (n = 192,210,188)	42.8 (36.1 to 49.6)	38.0 (31.7 to 44.2)	42.5 (35.6 to 49.4)	
Week 96 (n = 190,210,189)	42.9 (36.1 to 49.7)	35.9 (29.8 to 41.9)	35.9 (29.2 to 42.5)	
Week 100 (n = 196,213,183)	43.9 (37.1 to 50.8)	33.0 (26.9 to 39.0)	40.9 (34.0 to 47.9)	

Notes:

[14] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Gaining ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[15]	248	
Units: Percentage of participants				
number (confidence interval 95%)				

Week 4 (n = 245,243,242)	29.4 (23.9 to 34.9)	28.9 (23.3 to 34.5)	26.9 (21.3 to 32.4)	
Week 8 (n = 244,246,242)	38.2 (32.3 to 44.1)	42.2 (36.1 to 48.3)	33.1 (27.2 to 38.9)	
Week 12 (n = 242,241,236)	45.2 (39.0 to 51.4)	46.9 (40.7 to 53.1)	43.9 (37.7 to 50.1)	
Week 16 (n = 241,241,230)	52.3 (46.2 to 58.5)	51.4 (45.4 to 57.4)	41.7 (35.5 to 48.0)	
Week 20 (n = 233,239,230)	53.4 (47.2 to 59.6)	51.1 (44.9 to 57.4)	45.5 (39.2 to 51.8)	
Week 24 (n = 231,242,232)	57.8 (51.6 to 64.1)	53.1 (46.9 to 59.2)	49.3 (43.1 to 55.5)	
Week 28 (n = 223,232,222)	59.7 (53.4 to 66.1)	53.1 (46.9 to 59.4)	55.3 (49.0 to 61.6)	
Week 32 (n = 216,220,216)	61.2 (54.7 to 67.6)	50.6 (44.2 to 57.1)	55.7 (49.2 to 62.1)	
Week 36 (n = 212,220,209)	58.8 (52.3 to 65.2)	57.8 (51.5 to 64.0)	59.6 (53.1 to 66.0)	
Week 40 (n = 213,222,211)	61.3 (55.0 to 67.7)	56.8 (50.6 to 63.1)	58.5 (52.2 to 64.9)	
Week 44 (n = 208,223,211)	61.6 (55.0 to 68.2)	56.8 (50.5 to 63.1)	61.1 (54.7 to 67.4)	
Week 48 (n = 199,224,212)	57.4 (50.6 to 64.2)	58.0 (51.7 to 64.2)	58.1 (51.7 to 64.6)	
Week 52 (n = 209,223,207)	60.9 (54.4 to 67.4)	61.6 (55.3 to 67.8)	60.0 (53.5 to 66.5)	
Week 56 (n = 209,224,200)	61.0 (54.6 to 67.4)	58.6 (52.3 to 64.9)	58.6 (51.9 to 65.3)	
Week 60 (n = 208,219,200)	57.9 (51.3 to 64.5)	57.1 (50.8 to 63.5)	56.2 (49.5 to 63.0)	
Week 64 (n = 205,228,203)	58.4 (51.8 to 65.0)	56.2 (49.9 to 62.5)	53.7 (46.9 to 60.4)	
Week 68 (n = 201,214,200)	58.9 (52.4 to 65.4)	54.4 (47.8 to 61.0)	60.7 (54.0 to 67.3)	
Week 72 (n = 191,205,196)	58.4 (51.5 to 65.4)	57.5 (51.0 to 64.1)	59.3 (52.5 to 66.0)	
Week 76 (n = 199,216,195)	58.2 (51.5 to 64.9)	54.0 (47.5 to 60.6)	57.5 (50.8 to 64.3)	
Week 80 (n = 189,210,193)	60.4 (53.6 to 67.2)	58.1 (51.6 to 64.6)	57.0 (50.2 to 63.9)	
Week 84 (n = 194,209,199)	55.9 (49.1 to 62.8)	56.5 (50.0 to 63.1)	57.1 (50.3 to 63.8)	
Week 88 (n = 194,211,191)	57.1 (50.3 to 63.9)	53.6 (46.9 to 60.3)	58.8 (52.0 to 65.6)	
Week 92 (n = 192,210,188)	58.8 (51.9 to 65.6)	57.0 (50.4 to 63.5)	60.5 (53.7 to 67.2)	
Week 96 (n = 190,210,189)	64.7 (58.0 to 71.4)	58.4 (51.9 to 65.0)	59.8 (52.9 to 66.7)	
Week 100 (n = 196,213,183)	63.0 (56.5 to 69.5)	55.2 (48.7 to 61.7)	66.2 (59.5 to 72.8)	

Notes:

[15] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥5 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Gaining ≥5 Letters in BCVA From

	Baseline in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[16]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,243,242)	57.9 (51.8 to 64.1)	62.2 (56.1 to 68.3)	58.3 (52.1 to 64.5)	
Week 8 (n = 244,246,242)	65.6 (59.7 to 71.4)	68.3 (62.5 to 74.1)	65.3 (59.3 to 71.2)	
Week 12 (n = 242,241,236)	71.1 (65.4 to 76.8)	74.7 (69.2 to 80.2)	72.4 (66.7 to 78.1)	
Week 16 (n = 241,241,230)	76.4 (71.1 to 81.7)	75.5 (70.1 to 80.8)	69.1 (63.2 to 75.1)	
Week 20 (n = 233,239,230)	76.5 (71.1 to 81.9)	80.4 (75.4 to 85.3)	72.5 (66.8 to 78.3)	
Week 24 (n = 231,242,232)	78.0 (72.7 to 83.3)	77.4 (72.2 to 82.6)	72.2 (66.5 to 77.9)	
Week 28 (n = 223,232,222)	77.2 (71.7 to 82.7)	79.7 (74.6 to 84.9)	76.9 (71.5 to 82.3)	
Week 32 (n = 216,220,216)	81.1 (75.9 to 86.3)	80.0 (74.8 to 85.3)	77.1 (71.6 to 82.6)	
Week 36 (n = 212,220,209)	77.4 (71.8 to 83.0)	81.4 (76.2 to 86.5)	79.3 (73.9 to 84.7)	
Week 40 (n = 213,222,211)	78.6 (73.1 to 84.0)	79.7 (74.4 to 85.0)	81.5 (76.2 to 86.7)	
Week 44 (n = 208,223,211)	83.7 (78.7 to 88.6)	79.3 (74.0 to 84.5)	85.8 (81.1 to 90.5)	
Week 48 (n = 199,224,212)	79.9 (74.4 to 85.4)	84.0 (79.2 to 88.7)	79.0 (73.6 to 84.4)	
Week 52 (n = 209,223,207)	81.8 (76.6 to 87.0)	80.3 (75.1 to 85.4)	79.4 (73.9 to 84.8)	
Week 56 (n = 209,224,200)	78.2 (72.7 to 83.7)	78.7 (73.4 to 84.0)	82.4 (77.2 to 87.7)	
Week 60 (n = 208,219,200)	75.1 (69.4 to 80.9)	77.3 (71.8 to 82.8)	80.3 (74.8 to 85.7)	
Week 64 (n = 205,228,203)	76.3 (70.5 to 82.1)	79.0 (73.7 to 84.2)	73.0 (66.9 to 79.0)	

Week 68 (n = 201,214,200)	75.4 (69.6 to 81.3)	77.6 (72.0 to 83.2)	78.2 (72.6 to 83.9)	
Week 72 (n = 191,205,196)	78.4 (72.8 to 84.1)	77.7 (72.1 to 83.4)	77.3 (71.5 to 83.1)	
Week 76 (n = 199,216,195)	75.6 (69.7 to 81.5)	76.1 (70.4 to 81.7)	73.6 (67.5 to 79.8)	
Week 80 (n = 189,210,193)	75.2 (69.3 to 81.1)	78.2 (72.6 to 83.8)	78.5 (72.7 to 84.2)	
Week 84 (n = 194,209,199)	72.3 (66.1 to 78.5)	80.5 (75.2 to 85.9)	76.3 (70.5 to 82.2)	
Week 88 (n = 194,211,191)	73.9 (67.8 to 80.0)	75.9 (70.2 to 81.7)	80.6 (75.1 to 86.2)	
Week 92 (n = 192,210,188)	73.7 (67.6 to 79.9)	77.4 (71.8 to 83.0)	80.2 (74.5 to 85.9)	
Week 96 (n = 190,210,189)	78.7 (73.0 to 84.4)	77.5 (72.0 to 83.0)	76.9 (70.9 to 82.8)	
Week 100 (n = 196,213,183)	79.0 (73.4 to 84.6)	78.2 (72.7 to 83.7)	81.7 (76.2 to 87.3)	

Notes:

[16] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥0 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Gaining ≥0 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[17]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,243,242)	84.9 (80.5 to 89.3)	88.5 (84.5 to 92.5)	88.8 (84.9 to 92.8)	

Week 8 (n = 244,246,242)	89.3 (85.4 to 93.1)	90.6 (87.0 to 94.2)	90.1 (86.3 to 93.9)	
Week 12 (n = 242,241,236)	90.1 (86.4 to 93.9)	92.9 (89.7 to 96.1)	90.6 (86.9 to 94.3)	
Week 16 (n = 241,241,230)	91.3 (87.7 to 94.8)	90.9 (87.3 to 94.5)	91.3 (87.7 to 94.9)	
Week 20 (n = 233,239,230)	91.9 (88.4 to 95.4)	92.9 (89.6 to 96.1)	93.9 (90.9 to 97.0)	
Week 24 (n = 231,242,232)	90.9 (87.3 to 94.6)	92.6 (89.3 to 95.9)	92.2 (88.7 to 95.7)	
Week 28 (n = 223,232,222)	91.9 (88.4 to 95.5)	95.2 (92.5 to 98.0)	94.5 (91.6 to 97.5)	
Week 32 (n = 216,220,216)	91.2 (87.4 to 95.0)	90.5 (86.6 to 94.4)	93.5 (90.2 to 96.8)	
Week 36 (n = 212,220,209)	91.5 (87.8 to 95.3)	90.5 (86.7 to 94.4)	96.2 (93.7 to 98.8)	
Week 40 (n = 213,222,211)	91.6 (87.9 to 95.3)	92.8 (89.5 to 96.2)	94.8 (91.9 to 97.8)	
Week 44 (n = 208,223,211)	91.8 (88.1 to 95.6)	91.5 (87.8 to 95.1)	95.3 (92.4 to 98.1)	
Week 48 (n = 199,224,212)	93.5 (90.0 to 96.9)	91.1 (87.5 to 94.8)	92.9 (89.4 to 96.4)	
Week 52 (n = 209,223,207)	94.3 (91.1 to 97.4)	91.0 (87.3 to 94.8)	93.3 (89.9 to 96.7)	
Week 56 (n = 209,224,200)	93.9 (90.7 to 97.1)	92.4 (89.0 to 95.9)	91.0 (87.1 to 95.0)	
Week 60 (n = 208,219,200)	88.5 (84.2 to 92.8)	87.8 (83.4 to 92.1)	93.0 (89.5 to 96.5)	
Week 64 (n = 205,228,203)	90.5 (86.5 to 94.4)	89.5 (85.5 to 93.5)	88.5 (84.1 to 92.9)	
Week 68 (n = 201,214,200)	89.6 (85.4 to 93.8)	90.7 (86.8 to 94.6)	90.5 (86.4 to 94.5)	
Week 72 (n = 191,205,196)	89.1 (84.7 to 93.5)	89.7 (85.6 to 93.9)	87.7 (83.1 to 92.3)	
Week 76 (n = 199,216,195)	89.6 (85.5 to 93.8)	88.5 (84.2 to 92.7)	89.7 (85.4 to 94.0)	
Week 80 (n = 189,210,193)	86.4 (81.5 to 91.2)	89.7 (85.6 to 93.8)	88.9 (84.4 to 93.3)	
Week 84 (n = 194,209,199)	87.6 (83.0 to 92.2)	91.1 (87.3 to 94.9)	88.0 (83.5 to 92.5)	
Week 88 (n = 194,211,191)	84.7 (79.7 to 89.7)	90.2 (86.2 to 94.1)	90.6 (86.4 to 94.7)	
Week 92 (n = 192,210,188)	85.5 (80.6 to 90.5)	86.3 (81.7 to 90.9)	88.9 (84.3 to 93.4)	
Week 96 (n = 190,210,189)	84.8 (79.8 to 89.9)	87.8 (83.4 to 92.2)	89.3 (84.9 to 93.7)	
Week 100 (n = 196,213,183)	85.3 (80.4 to 90.3)	89.0 (84.9 to 93.1)	91.8 (87.8 to 95.7)	

Notes:

[17] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Avoiding a Loss of ≥15, ≥10, or ≥5 Letters in BCVA from Baseline in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT Population

End point title	Percentage of Participants Avoiding a Loss of ≥15, ≥10, or ≥5 Letters in BCVA from Baseline in the Study Eye Averaged Over

	Weeks 48, 52, and 56, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	268	293	279	
Units: Percentage of participants				
number (confidence interval 95%)				
Avoiding a Loss of ≥15 Letters	98.9 (97.6 to 100.0)	98.7 (97.4 to 100.0)	98.6 (97.2 to 99.9)	
Avoiding a Loss of ≥10 Letters	98.1 (96.5 to 99.7)	98.0 (96.4 to 99.6)	98.2 (96.7 to 99.7)	
Avoiding a Loss of ≥5 Letters	96.7 (94.5 to 98.8)	97.0 (95.0 to 98.9)	95.4 (93.0 to 97.8)	

Statistical analyses

Statistical analysis title	Avoiding a Loss of ≥15 Letters: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants avoiding a loss of ≥15 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	2.1

Statistical analysis title	Avoiding a Loss of ≥15 Letters: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants avoiding a loss of ≥15 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1.9

Statistical analysis title	Avoiding a Loss of ≥10 Letters: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants avoiding a loss of ≥10 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	2.1

Statistical analysis title	Avoiding a Loss of ≥10 Letters: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants avoiding a loss of ≥10 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	1.9

Statistical analysis title	Avoiding a Loss of ≥5 Letters: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants avoiding a loss of ≥5 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	4.5

Statistical analysis title	Avoiding a Loss of ≥5 Letters: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants avoiding a loss of ≥5 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	4.6

Secondary: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted estimates of the percentage of participants avoiding a loss of letters in BCVA from baseline were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values

were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307, 306, 309)	99.4 (98.5 to 100.0)	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)	
Week 8 (n = 305, 311, 309)	99.7 (99.1 to 100.0)	100.0 (100.0 to 100.0)	99.7 (99.1 to 100.0)	
Week 12 (n = 305, 303, 302)	99.7 (99.0 to 100.0)	99.7 (99.1 to 100.0)	99.7 (99.1 to 100.0)	
Week 16 (n = 300,304,296)	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)	99.7 (99.0 to 100.0)	
Week 20 (n = 294,302,295)	99.6 (99.0 to 100.0)	99.3 (98.4 to 100.0)	99.3 (98.4 to 100.0)	
Week 24 (n = 293,306,297)	99.3 (98.4 to 100.0)	99.3 (98.4 to 100.0)	99.3 (98.4 to 100.0)	
Week 28 (n = 284,295,287)	99.7 (99.0 to 100.0)	99.3 (98.4 to 100.0)	99.0 (97.8 to 100.0)	
Week 32 (n = 277,284,280)	98.9 (97.7 to 100.0)	98.9 (97.8 to 100.0)	98.5 (97.2 to 99.9)	
Week 36 (n = 275,281,275)	99.3 (98.3 to 100.0)	99.0 (97.9 to 100.0)	98.9 (97.8 to 100.0)	
Week 40 (n = 275,286,274)	98.9 (97.6 to 100.0)	98.6 (97.3 to 99.9)	99.3 (98.3 to 100.0)	
Week 44 (n = 269,286,272)	99.6 (98.8 to 100.0)	99.0 (97.8 to 100.0)	98.5 (97.2 to 99.9)	
Week 48 (n = 255,286,278)	99.6 (98.8 to 100.0)	98.3 (96.8 to 99.8)	99.3 (98.3 to 100.0)	
Week 52 (n = 267,281,271)	98.4 (96.9 to 99.9)	98.9 (97.8 to 100.0)	99.6 (99.0 to 100.0)	
Week 56 (n = 267,283,261)	98.5 (97.0 to 100.0)	99.3 (98.4 to 100.0)	98.9 (97.6 to 100.0)	
Week 60 (n = 261,277,255)	98.8 (97.5 to 100.0)	98.9 (97.7 to 100.0)	98.0 (96.4 to 99.7)	
Week 64 (n = 258,290,259)	98.4 (96.9 to 99.9)	98.3 (96.8 to 99.8)	96.9 (94.8 to 99.0)	
Week 68 (n = 254,272,255)	98.4 (96.9 to 99.9)	98.2 (96.6 to 99.8)	97.6 (95.8 to 99.5)	
Week 72 (n = 245,261,250)	98.9 (97.6 to 100.0)	98.8 (97.6 to 100.0)	97.6 (95.8 to 99.5)	
Week 76 (n = 257,273,251)	96.9 (94.8 to 99.0)	98.2 (96.6 to 99.8)	97.6 (95.7 to 99.5)	
Week 80 (n = 247,269,250)	96.4 (94.1 to 98.7)	98.1 (96.5 to 99.7)	97.5 (95.6 to 99.5)	
Week 84 (n = 253,265,255)	96.2 (93.9 to 98.5)	99.3 (98.3 to 100.0)	97.3 (95.3 to 99.3)	
Week 88 (n = 254,267,247)	94.9 (92.2 to 97.6)	98.1 (96.5 to 99.7)	97.6 (95.7 to 99.5)	

Week 92 (n = 249,269,242)	96.0 (93.6 to 98.4)	97.4 (95.5 to 99.3)	97.1 (95.0 to 99.2)	
Week 96 (n = 244,267,241)	95.5 (92.9 to 98.1)	97.8 (96.0 to 99.5)	98.4 (96.8 to 99.9)	
Week 100 (n = 251,271,237)	96.1 (93.7 to 98.4)	96.3 (94.1 to 98.5)	96.1 (93.7 to 98.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted estimates of the percentage of participants avoiding a loss of letters in BCVA from baseline were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,306,309)	99.4 (98.5 to 100.0)	99.3 (98.4 to 100.0)	99.4 (98.5 to 100.0)	
Week 8 (n = 305,311,309)	99.0 (98.0 to 100.0)	99.4 (98.5 to 100.0)	99.0 (98.0 to 100.0)	
Week 12 (n = 305,303,302)	98.7 (97.5 to 99.9)	99.0 (98.0 to 100.0)	99.3 (98.5 to 100.0)	
Week 16 (n = 300,304,296)	99.7 (99.0 to 100.0)	99.7 (99.0 to 100.0)	99.3 (98.4 to 100.0)	
Week 20 (n = 294,302,295)	98.6 (97.3 to 99.9)	99.0 (97.9 to 100.0)	99.0 (97.9 to 100.0)	
Week 24 (n = 293,306,297)	98.2 (96.7 to 99.8)	99.3 (98.4 to 100.0)	98.7 (97.4 to 99.9)	
Week 28 (n = 284,295,287)	99.7 (99.0 to 100.0)	99.0 (97.8 to 100.0)	99.0 (97.8 to 100.0)	
Week 32 (n = 277,284,280)	98.5 (97.1 to 99.9)	98.6 (97.3 to 99.9)	97.5 (95.7 to 99.2)	

Week 36 (n = 275,281,275)	98.9 (97.7 to 100.0)	98.7 (97.4 to 99.9)	98.2 (96.7 to 99.8)	
Week 40 (n = 275,286,274)	98.1 (96.5 to 99.7)	97.9 (96.3 to 99.6)	98.6 (97.2 to 99.9)	
Week 44 (n = 269,286,272)	98.5 (97.0 to 100.0)	98.6 (97.3 to 100.0)	98.2 (96.6 to 99.7)	
Week 48 (n = 255,286,278)	98.4 (96.8 to 99.9)	96.5 (94.5 to 98.6)	98.9 (97.8 to 100.0)	
Week 52 (n = 267,281,271)	97.7 (95.9 to 99.5)	98.2 (96.7 to 99.8)	98.6 (97.2 to 99.9)	
Week 56 (n = 267,283,261)	98.5 (97.0 to 100.0)	98.6 (97.2 to 99.9)	97.0 (95.0 to 99.0)	
Week 60 (n = 261,277,255)	98.0 (96.3 to 99.7)	97.1 (95.2 to 99.1)	96.5 (94.3 to 98.7)	
Week 64 (n = 258,290,259)	97.7 (95.9 to 99.5)	97.3 (95.4 to 99.1)	96.5 (94.3 to 98.7)	
Week 68 (n = 254,272,255)	96.4 (94.1 to 98.7)	96.3 (94.1 to 98.5)	96.0 (93.6 to 98.4)	
Week 72 (n = 245,261,250)	96.4 (94.1 to 98.7)	98.1 (96.4 to 99.7)	97.2 (95.2 to 99.2)	
Week 76 (n = 257,273,251)	95.7 (93.2 to 98.1)	97.4 (95.5 to 99.3)	96.8 (94.6 to 99.0)	
Week 80 (n = 247,269,250)	95.2 (92.5 to 97.8)	96.7 (94.6 to 98.8)	95.9 (93.4 to 98.3)	
Week 84 (n = 253,265,255)	94.6 (91.9 to 97.3)	98.5 (97.1 to 99.9)	95.3 (92.7 to 97.9)	
Week 88 (n = 254,267,247)	93.3 (90.3 to 96.4)	97.0 (95.0 to 99.0)	95.1 (92.4 to 97.7)	
Week 92 (n = 249,269,242)	93.6 (90.6 to 96.6)	94.8 (92.1 to 97.4)	95.4 (92.9 to 98.0)	
Week 96 (n = 244,267,241)	93.4 (90.3 to 96.5)	95.5 (93.0 to 98.0)	95.3 (92.7 to 98.0)	
Week 100 (n = 251,271,237)	94.8 (92.2 to 97.5)	94.9 (92.3 to 97.5)	94.8 (92.0 to 97.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA From Baseline in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted estimates of the percentage of participants avoiding a loss of letters in BCVA from baseline were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307, 306, 309)	95.1 (92.8 to 97.5)	97.4 (95.6 to 99.2)	97.7 (96.1 to 99.4)	
Week 8 (n = 305, 311, 309)	96.7 (94.7 to 98.7)	97.1 (95.3 to 98.9)	97.1 (95.2 to 98.9)	
Week 12 (n = 305, 303, 302)	97.4 (95.6 to 99.2)	96.7 (94.7 to 98.7)	97.0 (95.1 to 98.9)	
Week 16 (n = 300,304,296)	97.7 (96.0 to 99.4)	97.7 (96.0 to 99.4)	96.6 (94.6 to 98.7)	
Week 20 (n = 294,302,295)	96.9 (95.0 to 98.9)	96.7 (94.7 to 98.7)	97.3 (95.5 to 99.1)	
Week 24 (n = 293,306,297)	96.5 (94.4 to 98.6)	96.4 (94.4 to 98.5)	96.4 (94.3 to 98.4)	
Week 28 (n = 284,295,287)	96.1 (93.9 to 98.4)	97.3 (95.5 to 99.1)	97.9 (96.3 to 99.5)	
Week 32 (n = 277,284,280)	96.4 (94.3 to 98.6)	96.5 (94.4 to 98.6)	95.0 (92.5 to 97.5)	
Week 36 (n = 275,281,275)	97.5 (95.7 to 99.3)	96.6 (94.5 to 98.6)	97.5 (95.7 to 99.3)	
Week 40 (n = 275,286,274)	96.7 (94.6 to 98.8)	95.9 (93.6 to 98.1)	96.7 (94.7 to 98.8)	
Week 44 (n = 269,286,272)	96.3 (94.0 to 98.5)	95.8 (93.5 to 98.1)	96.3 (94.1 to 98.5)	
Week 48 (n = 255,286,278)	96.4 (94.2 to 98.7)	95.2 (92.7 to 97.6)	96.1 (93.8 to 98.3)	
Week 52 (n = 267,281,271)	96.2 (93.9 to 98.4)	94.7 (92.1 to 97.3)	96.7 (94.5 to 98.8)	
Week 56 (n = 267,283,261)	95.6 (93.1 to 98.0)	96.8 (94.7 to 98.8)	96.6 (94.5 to 98.7)	
Week 60 (n = 261,277,255)	95.0 (92.3 to 97.6)	94.6 (92.0 to 97.2)	95.3 (92.8 to 97.8)	
Week 64 (n = 258,290,259)	95.9 (93.5 to 98.2)	92.8 (89.8 to 95.8)	93.3 (90.3 to 96.3)	
Week 68 (n = 254,272,255)	94.8 (92.1 to 97.6)	93.7 (90.8 to 96.6)	94.9 (92.1 to 97.6)	
Week 72 (n = 245,261,250)	94.0 (91.0 to 96.9)	94.6 (91.9 to 97.4)	92.9 (89.7 to 96.0)	
Week 76 (n = 257,273,251)	93.7 (90.8 to 96.7)	92.3 (89.2 to 95.5)	94.7 (92.0 to 97.5)	
Week 80 (n = 247,269,250)	92.4 (89.1 to 95.7)	93.8 (90.9 to 96.6)	93.4 (90.4 to 96.4)	
Week 84 (n = 253,265,255)	92.7 (89.6 to 95.8)	93.3 (90.3 to 96.2)	92.9 (89.9 to 96.0)	
Week 88 (n = 254,267,247)	89.9 (86.2 to 93.5)	91.7 (88.5 to 95.0)	93.4 (90.4 to 96.5)	
Week 92 (n = 249,269,242)	91.7 (88.3 to 95.1)	90.7 (87.3 to 94.2)	92.9 (89.7 to 96.1)	
Week 96 (n = 244,267,241)	90.1 (86.4 to 93.8)	91.1 (87.7 to 94.5)	92.8 (89.5 to 96.1)	
Week 100 (n = 251,271,237)	91.6 (88.2 to 95.0)	90.4 (87.0 to 93.9)	93.6 (90.5 to 96.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Avoiding a Loss of ≥15, ≥10, or ≥5 Letters in BCVA from Baseline in the Study Eye Averaged Over Weeks 48, 52, and 56, Treatment-Naive Population

End point title	Percentage of Participants Avoiding a Loss of ≥15, ≥10, or ≥5 Letters in BCVA from Baseline in the Study Eye Averaged Over Weeks 48, 52, and 56, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	208	231	213	
Units: Percentage of participants				
number (confidence interval 95%)				
Avoiding a Loss of ≥15 Letters	98.5 (96.9 to 100.0)	98.7 (97.2 to 100.0)	98.6 (97.0 to 100.0)	
Avoiding a Loss of ≥10 Letters	98.1 (96.2 to 99.9)	97.8 (96.0 to 99.7)	98.1 (96.3 to 99.9)	
Avoiding a Loss of ≥5 Letters	97.6 (95.5 to 99.7)	97.4 (95.4 to 99.4)	96.2 (93.7 to 98.8)	

Statistical analyses

Statistical analysis title	Avoiding a Loss of ≥15 Letters: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants avoiding a loss of ≥15 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	2.2

Statistical analysis title	Avoiding a Loss of ≥15 Letters: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants avoiding a loss of ≥15 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2.2

Statistical analysis title	Avoiding a Loss of ≥10 Letters: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants avoiding a loss of ≥10 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	2.6

Statistical analysis title	Avoiding a Loss of ≥10 Letters: Arm B vs. Arm C
Statistical analysis description: This is the difference in percentage of participants avoiding a loss of ≥10 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	2.3

Statistical analysis title	Avoiding a Loss of ≥5 Letters: Arm A vs. Arm C
Statistical analysis description: This is the difference in percentage of participants avoiding a loss of ≥5 letters in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	4.7

Statistical analysis title	Avoiding a Loss of ≥5 Letters: Arm B vs. Arm C
Statistical analysis description: This is the difference in percentage of participants avoiding a loss of ≥5 letters in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population

Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	4.4

Secondary: Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Avoiding a Loss of ≥15 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted estimates of the percentage of participants avoiding a loss of letters in BCVA from baseline were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[18]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,243,242)	99.6 (98.8 to 100.0)	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)	
Week 8 (n = 244,246,242)	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)	99.6 (98.8 to 100.0)	
Week 12 (n = 242,241,236)	100.0 (100.0 to 100.0)	99.6 (98.8 to 100.0)	99.6 (98.8 to 100.0)	
Week 16 (n = 241,241,230)	100.0 (100.0 to 100.0)	100.0 (100.0 to 100.0)	99.6 (98.7 to 100.0)	
Week 20 (n = 233,239,230)	100.0 (100.0 to 100.0)	99.2 (98.0 to 100.0)	99.6 (98.7 to 100.0)	
Week 24 (n = 231,242,232)	99.2 (98.0 to 100.0)	99.2 (98.0 to 100.0)	99.6 (98.8 to 100.0)	
Week 28 (n = 223,232,222)	99.6 (98.8 to 100.0)	99.6 (98.7 to 100.0)	99.1 (97.9 to 100.0)	

Week 32 (n = 216,220,216)	98.6 (97.1 to 100.0)	99.1 (97.8 to 100.0)	99.1 (97.8 to 100.0)	
Week 36 (n = 212,220,209)	99.0 (97.7 to 100.0)	99.2 (98.1 to 100.0)	99.1 (97.8 to 100.0)	
Week 40 (n = 213,222,211)	99.0 (97.7 to 100.0)	99.1 (97.9 to 100.0)	99.5 (98.6 to 100.0)	
Week 44 (n = 208,223,211)	99.5 (98.5 to 100.0)	99.1 (97.9 to 100.0)	99.1 (97.8 to 100.0)	
Week 48 (n = 199,224,212)	99.5 (98.5 to 100.0)	98.3 (96.6 to 99.9)	99.5 (98.6 to 100.0)	
Week 52 (n = 209,223,207)	99.0 (97.6 to 100.0)	98.6 (97.1 to 100.0)	100.0 (100.0 to 100.0)	
Week 56 (n = 209,224,200)	98.1 (96.2 to 99.9)	99.1 (97.9 to 100.0)	98.5 (96.9 to 100.0)	
Week 60 (n = 208,219,200)	99.0 (97.7 to 100.0)	98.6 (97.1 to 100.0)	98.5 (96.9 to 100.0)	
Week 64 (n = 205,228,203)	99.0 (97.7 to 100.0)	98.2 (96.5 to 99.9)	97.0 (94.7 to 99.4)	
Week 68 (n = 201,214,200)	99.0 (97.6 to 100.0)	97.7 (95.7 to 99.7)	97.5 (95.4 to 99.7)	
Week 72 (n = 191,205,196)	99.5 (98.5 to 100.0)	98.5 (96.9 to 100.0)	97.5 (95.3 to 99.7)	
Week 76 (n = 199,216,195)	97.5 (95.3 to 99.7)	98.1 (96.3 to 99.9)	97.9 (95.8 to 99.9)	
Week 80 (n = 189,210,193)	96.8 (94.3 to 99.3)	98.1 (96.3 to 99.9)	97.9 (95.8 to 99.9)	
Week 84 (n = 194,209,199)	96.9 (94.5 to 99.3)	99.1 (97.9 to 100.0)	97.0 (94.7 to 99.4)	
Week 88 (n = 194,211,191)	94.9 (91.8 to 98.0)	98.1 (96.3 to 99.9)	97.4 (95.2 to 99.6)	
Week 92 (n = 192,210,188)	96.4 (93.7 to 99.0)	97.2 (94.9 to 99.4)	97.4 (95.1 to 99.6)	
Week 96 (n = 190,210,189)	95.3 (92.3 to 98.3)	97.7 (95.7 to 99.7)	98.5 (96.8 to 100.0)	
Week 100 (n = 196,213,183)	95.5 (92.6 to 98.4)	96.3 (93.7 to 98.8)	96.7 (94.1 to 99.3)	

Notes:

[18] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Avoiding a Loss of ≥10 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted estimates of the percentage of participants avoiding a loss of letters in BCVA from baseline were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[19]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,243,242)	99.6 (98.8 to 100.0)	99.2 (98.0 to 100.0)	99.2 (98.0 to 100.0)	
Week 8 (n = 244,246,242)	99.2 (98.0 to 100.0)	99.2 (98.1 to 100.0)	98.8 (97.4 to 100.0)	
Week 12 (n = 242,241,236)	99.2 (98.1 to 100.0)	99.2 (98.1 to 100.0)	99.2 (98.0 to 100.0)	
Week 16 (n = 241,241,230)	99.6 (98.8 to 100.0)	99.6 (98.8 to 100.0)	99.1 (97.9 to 100.0)	
Week 20 (n = 233,239,230)	98.7 (97.3 to 100.0)	98.8 (97.3 to 100.0)	99.1 (97.9 to 100.0)	
Week 24 (n = 231,242,232)	97.8 (95.9 to 99.7)	99.2 (98.0 to 100.0)	99.6 (98.8 to 100.0)	
Week 28 (n = 223,232,222)	99.6 (98.8 to 100.0)	99.1 (97.9 to 100.0)	99.1 (97.9 to 100.0)	
Week 32 (n = 216,220,216)	98.2 (96.4 to 99.9)	99.1 (97.8 to 100.0)	98.6 (97.0 to 100.0)	
Week 36 (n = 212,220,209)	98.6 (97.0 to 100.0)	98.7 (97.3 to 100.0)	98.6 (97.0 to 100.0)	
Week 40 (n = 213,222,211)	98.5 (96.9 to 100.0)	98.7 (97.2 to 100.0)	98.6 (97.0 to 100.0)	
Week 44 (n = 208,223,211)	98.1 (96.2 to 99.9)	98.7 (97.2 to 100.0)	98.6 (97.0 to 100.0)	
Week 48 (n = 199,224,212)	99.0 (97.5 to 100.0)	96.5 (94.1 to 98.9)	99.5 (98.6 to 100.0)	
Week 52 (n = 209,223,207)	98.5 (96.9 to 100.0)	97.8 (95.8 to 99.7)	99.0 (97.7 to 100.0)	
Week 56 (n = 209,224,200)	98.1 (96.2 to 99.9)	98.7 (97.2 to 100.0)	96.6 (94.1 to 99.1)	
Week 60 (n = 208,219,200)	98.5 (96.9 to 100.0)	96.4 (93.9 to 98.8)	97.0 (94.6 to 99.4)	
Week 64 (n = 205,228,203)	98.6 (96.9 to 100.0)	96.9 (94.7 to 99.2)	97.0 (94.7 to 99.4)	
Week 68 (n = 201,214,200)	97.0 (94.6 to 99.4)	95.4 (92.6 to 98.2)	95.5 (92.6 to 98.4)	
Week 72 (n = 191,205,196)	97.9 (95.8 to 99.9)	98.1 (96.2 to 99.9)	97.5 (95.3 to 99.7)	
Week 76 (n = 199,216,195)	96.0 (93.2 to 98.7)	97.2 (95.0 to 99.4)	96.4 (93.8 to 99.0)	
Week 80 (n = 189,210,193)	95.8 (92.9 to 98.6)	96.3 (93.7 to 98.8)	96.3 (93.6 to 99.0)	
Week 84 (n = 194,209,199)	95.9 (92.9 to 98.6)	98.6 (97.1 to 100.0)	95.5 (92.6 to 98.4)	
Week 88 (n = 194,211,191)	93.9 (90.5 to 97.2)	96.7 (94.4 to 99.1)	95.3 (92.3 to 98.3)	
Week 92 (n = 192,210,188)	93.8 (90.4 to 97.2)	94.8 (91.8 to 97.8)	95.8 (93.0 to 98.6)	

Week 96 (n = 190,210,189)	92.7 (89.0 to 96.4)	96.2 (93.6 to 98.8)	95.7 (92.9 to 98.6)	
Week 100 (n = 196,213,183)	94.5 (91.3 to 97.6)	94.5 (91.4 to 97.5)	96.1 (93.3 to 98.9)	

Notes:

[19] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Avoiding a Loss of ≥5 Letters in BCVA From Baseline in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The weighted estimates of the percentage of participants avoiding a loss of letters in BCVA from baseline were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[20]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,243,242)	95.5 (92.9 to 98.1)	97.1 (95.0 to 99.2)	97.5 (95.6 to 99.5)	
Week 8 (n = 244,246,242)	96.3 (93.9 to 98.6)	97.1 (95.1 to 99.2)	96.3 (93.9 to 98.7)	
Week 12 (n = 242,241,236)	97.5 (95.6 to 99.5)	97.1 (95.0 to 99.2)	97.0 (94.9 to 99.2)	
Week 16 (n = 241,241,230)	97.1 (95.0 to 99.2)	98.3 (96.7 to 99.9)	97.0 (94.7 to 99.2)	
Week 20 (n = 233,239,230)	96.6 (94.3 to 98.9)	96.2 (93.8 to 98.6)	97.8 (96.0 to 99.7)	
Week 24 (n = 231,242,232)	96.1 (93.6 to 98.6)	97.1 (95.1 to 99.2)	97.4 (95.4 to 99.5)	
Week 28 (n = 223,232,222)	96.8 (94.5 to 99.1)	97.8 (96.0 to 99.7)	98.2 (96.4 to 99.9)	
Week 32 (n = 216,220,216)	96.8 (94.5 to 99.1)	96.4 (93.9 to 98.8)	95.8 (93.1 to 98.5)	
Week 36 (n = 212,220,209)	97.2 (95.0 to 99.4)	96.5 (94.1 to 98.9)	98.1 (96.3 to 99.9)	

Week 40 (n = 213,222,211)	96.7 (94.3 to 99.1)	96.9 (94.7 to 99.1)	97.2 (95.0 to 99.4)	
Week 44 (n = 208,223,211)	96.2 (93.6 to 98.8)	96.0 (93.4 to 98.5)	97.7 (95.6 to 99.7)	
Week 48 (n = 199,224,212)	96.4 (93.9 to 99.0)	95.6 (93.0 to 98.3)	96.2 (93.7 to 98.8)	
Week 52 (n = 209,223,207)	97.5 (95.4 to 99.7)	94.6 (91.7 to 97.6)	98.0 (96.2 to 99.9)	
Week 56 (n = 209,224,200)	96.7 (94.2 to 99.1)	97.8 (95.8 to 99.7)	96.6 (94.1 to 99.1)	
Week 60 (n = 208,219,200)	95.7 (92.9 to 98.4)	94.1 (91.1 to 97.2)	95.5 (92.6 to 98.4)	
Week 64 (n = 205,228,203)	96.2 (93.7 to 98.8)	92.1 (88.6 to 95.6)	94.1 (90.8 to 97.3)	
Week 68 (n = 201,214,200)	95.0 (92.0 to 98.0)	93.0 (89.6 to 96.4)	94.0 (90.7 to 97.3)	
Week 72 (n = 191,205,196)	94.8 (91.7 to 97.9)	94.2 (90.9 to 97.4)	92.4 (88.7 to 96.1)	
Week 76 (n = 199,216,195)	94.0 (90.7 to 97.3)	93.2 (89.9 to 96.5)	93.8 (90.4 to 97.2)	
Week 80 (n = 189,210,193)	92.7 (89.0 to 96.4)	94.5 (91.4 to 97.5)	94.1 (90.8 to 97.5)	
Week 84 (n = 194,209,199)	93.8 (90.4 to 97.2)	93.9 (90.7 to 97.1)	93.5 (90.0 to 96.9)	
Week 88 (n = 194,211,191)	90.8 (86.7 to 94.8)	92.1 (88.5 to 95.7)	93.7 (90.2 to 97.1)	
Week 92 (n = 192,210,188)	91.3 (87.4 to 95.3)	90.6 (86.7 to 94.5)	93.1 (89.4 to 96.7)	
Week 96 (n = 190,210,189)	88.5 (84.0 to 93.0)	92.0 (88.4 to 95.7)	93.0 (89.4 to 96.7)	
Week 100 (n = 196,213,183)	90.4 (86.3 to 94.5)	91.7 (88.1 to 95.4)	94.5 (91.2 to 97.8)	

Notes:

[20] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point title	Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	268	294	279	208
Units: Percentage of participants				
number (confidence interval 95%)	38.3 (32.6 to 44.0)	32.4 (27.2 to 37.6)	33.5 (28.1 to 38.9)	38.1 (31.7 to 44.5)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	232	213		
Units: Percentage of participants				
number (confidence interval 95%)	34.4 (28.5 to 40.4)	35.5 (29.2 to 41.9)		

Statistical analyses

Statistical analysis title	ITT: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	12.7

Statistical analysis title	ITT: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W

Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	6.2

Statistical analysis title	TN: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	11.6

Statistical analysis title	TN: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	7.4

Secondary: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,308,309)	14.7 (11.0 to 18.5)	13.0 (9.4 to 16.7)	13.2 (9.5 to 16.9)	
Week 8 (n = 306,313,309)	17.3 (13.1 to 21.5)	20.4 (16.0 to 24.8)	18.1 (13.8 to 22.3)	
Week 12 (n = 306,305,302)	23.2 (18.5 to 27.8)	25.5 (20.8 to 30.3)	22.7 (18.1 to 27.3)	
Week 16 (n = 301,306,296)	27.3 (22.4 to 32.2)	28.0 (23.2 to 32.8)	25.8 (21.0 to 30.7)	
Week 20 (n = 294,304,295)	28.7 (23.7 to 33.8)	24.0 (19.3 to 28.8)	26.5 (21.7 to 31.4)	
Week 24 (n = 294,307,297)	33.3 (28.0 to 38.6)	29.1 (24.0 to 34.1)	27.6 (22.6 to 32.6)	
Week 28 (n = 285,295,287)	34.9 (29.4 to 40.3)	30.7 (25.6 to 35.8)	28.8 (23.6 to 34.0)	
Week 32 (n = 278,284,280)	39.0 (33.5 to 44.6)	30.4 (25.2 to 35.7)	27.5 (22.4 to 32.6)	
Week 36 (n = 275,282,275)	36.3 (30.9 to 41.8)	35.8 (30.4 to 41.2)	33.2 (27.9 to 38.5)	
Week 40 (n = 276,287,274)	41.0 (35.3 to 46.6)	34.2 (28.9 to 39.5)	34.5 (29.0 to 40.0)	
Week 44 (n = 270,287,272)	40.6 (35.0 to 46.3)	33.5 (28.1 to 38.8)	38.5 (32.9 to 44.1)	
Week 48 (n = 255,287,278)	36.6 (30.8 to 42.4)	32.6 (27.4 to 37.8)	33.9 (28.4 to 39.3)	
Week 52 (n = 268,282,271)	39.3 (33.7 to 45.0)	34.7 (29.3 to 40.2)	38.4 (32.7 to 44.1)	
Week 56 (n = 268,284,261)	43.4 (37.7 to 49.2)	33.2 (27.9 to 38.5)	40.3 (34.4 to 46.2)	

Week 60 (n = 262,277,255)	41.2 (35.3 to 47.0)	34.2 (28.8 to 39.6)	39.0 (33.2 to 44.8)	
Week 64 (n = 258,291,259)	44.4 (38.5 to 50.2)	31.6 (26.4 to 36.8)	35.0 (29.4 to 40.7)	
Week 68 (n = 255,273,255)	40.2 (34.4 to 46.0)	33.5 (27.9 to 39.0)	39.0 (33.2 to 44.8)	
Week 72 (n = 246,262,250)	41.0 (35.0 to 47.1)	34.4 (28.8 to 39.9)	36.1 (30.4 to 41.8)	
Week 76 (n = 257,274,251)	39.7 (34.0 to 45.5)	35.7 (30.2 to 41.3)	39.1 (33.2 to 44.9)	
Week 80 (n = 248,270,250)	43.4 (37.4 to 49.4)	32.8 (27.4 to 38.2)	38.7 (32.7 to 44.6)	
Week 84 (n = 253,266,255)	41.7 (35.9 to 47.5)	33.8 (28.2 to 39.4)	40.5 (34.7 to 46.4)	
Week 88 (n = 255,268,247)	42.6 (36.8 to 48.4)	32.5 (27.0 to 38.0)	41.7 (35.7 to 47.6)	
Week 92 (n = 250,269,242)	45.6 (39.7 to 51.6)	38.3 (32.7 to 43.9)	45.0 (38.9 to 51.2)	
Week 96 (n = 245,268,241)	46.0 (39.9 to 52.1)	37.2 (31.7 to 42.7)	40.6 (34.5 to 46.7)	
Week 100 (n = 252,272,237)	44.5 (38.4 to 50.5)	34.3 (28.8 to 39.7)	44.3 (38.1 to 50.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants Gaining ≥15 Letters in BCVA from Baseline or Achieving BCVA Snellen Equivalent of 20/20 or Better (BCVA ≥84 Letters) in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[21]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,245,242)	15.1 (10.8 to 19.3)	13.5 (9.4 to 17.6)	12.8 (8.6 to 17.0)	
Week 8 (n = 245,248,242)	17.0 (12.4 to 21.7)	22.2 (17.0 to 27.3)	17.7 (13.0 to 22.4)	
Week 12 (n = 243,243,236)	22.6 (17.4 to 27.8)	26.3 (21.0 to 31.6)	22.7 (17.6 to 27.9)	
Week 16 (n = 242,243,230)	26.1 (20.6 to 31.5)	30.0 (24.4 to 35.5)	26.1 (20.6 to 31.6)	
Week 20 (n = 233,241,230)	28.4 (22.7 to 34.1)	26.2 (20.7 to 31.7)	25.9 (20.5 to 31.4)	
Week 24 (n = 232,243,232)	34.2 (28.2 to 40.3)	30.5 (24.8 to 36.3)	27.3 (21.7 to 32.9)	
Week 28 (n = 224,232,222)	35.4 (29.1 to 41.6)	32.9 (27.0 to 38.9)	29.6 (23.7 to 35.6)	
Week 32 (n = 217,220,216)	38.4 (32.0 to 44.7)	31.5 (25.5 to 37.5)	28.9 (23.0 to 34.8)	
Week 36 (n = 212,221,209)	37.0 (30.7 to 43.3)	38.0 (31.9 to 44.2)	34.6 (28.5 to 40.8)	
Week 40 (n = 214,223,211)	41.4 (34.9 to 47.8)	36.4 (30.2 to 42.5)	34.6 (28.3 to 40.9)	
Week 44 (n = 209,224,211)	40.3 (33.8 to 46.7)	34.3 (28.2 to 40.4)	40.7 (34.2 to 47.2)	
Week 48 (n = 199,225,212)	36.7 (30.1 to 43.4)	34.9 (28.9 to 40.9)	36.5 (30.1 to 42.9)	
Week 52 (n = 210,224,207)	39.1 (32.6 to 45.6)	37.0 (30.8 to 43.2)	39.8 (33.2 to 46.4)	
Week 56 (n = 210,225,200)	44.7 (38.1 to 51.2)	35.2 (29.1 to 41.3)	41.7 (35.0 to 48.5)	
Week 60 (n = 209,219,200)	40.9 (34.3 to 47.5)	36.9 (30.6 to 43.2)	39.2 (32.7 to 45.8)	
Week 64 (n = 205,229,203)	44.0 (37.4 to 50.6)	33.6 (27.5 to 39.7)	35.4 (29.0 to 41.8)	
Week 68 (n = 202,215,200)	39.7 (33.2 to 46.2)	35.5 (29.1 to 41.9)	40.0 (33.4 to 46.6)	
Week 72 (n = 192,206,196)	40.0 (33.1 to 46.8)	37.7 (31.2 to 44.2)	38.3 (31.7 to 45.0)	
Week 76 (n = 199,217,195)	40.6 (34.0 to 47.2)	37.8 (31.4 to 44.2)	39.1 (32.4 to 45.8)	
Week 80 (n = 190,211,193)	44.9 (38.0 to 51.8)	37.3 (30.9 to 43.7)	40.9 (34.1 to 47.6)	
Week 84 (n = 194,210,199)	43.1 (36.5 to 49.8)	36.0 (29.6 to 42.4)	41.4 (34.8 to 48.1)	
Week 88 (n = 195,212,191)	42.3 (35.6 to 49.1)	33.5 (27.2 to 39.8)	41.5 (34.7 to 48.2)	
Week 92 (n = 193,210,188)	47.1 (40.2 to 54.0)	42.6 (36.1 to 49.2)	45.2 (38.2 to 52.1)	
Week 96 (n = 191,211,189)	44.6 (37.7 to 51.5)	39.5 (33.1 to 45.8)	41.4 (34.4 to 48.3)	
Week 100 (n = 197,214,183)	45.6 (38.7 to 52.5)	36.9 (30.6 to 43.2)	44.9 (37.8 to 52.0)	

Notes:

[21] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA ≥69 Letters) in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA ≥69 Letters) in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥69 vs. <69 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	268	293	279	208
Units: Percentage of participants				
number (confidence interval 95%)	73.2 (68.2 to 78.3)	71.6 (66.7 to 76.4)	68.5 (63.6 to 73.5)	73.6 (68.0 to 79.3)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	231	213		
Units: Percentage of participants				
number (confidence interval 95%)	74.2 (68.9 to 79.5)	72.1 (66.6 to 77.7)		

Statistical analyses

Statistical analysis title	ITT: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	11.8

Statistical analysis title	ITT: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	572
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	9.8

Statistical analysis title	TN: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	9.4

Statistical analysis title	TN: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	9.3

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

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA ≥69 Letters) in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥69 vs. <69 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,306,309)	56.7 (51.6 to 61.7)	57.8 (53.2 to 62.4)	54.4 (49.7 to 59.1)	
Week 8 (n = 305,311,309)	61.3 (56.4 to 66.2)	65.7 (61.1 to 70.3)	59.4 (54.7 to 64.1)	
Week 12 (n = 305,303,302)	68.0 (63.2 to 72.8)	67.8 (63.2 to 72.4)	65.2 (60.4 to 70.0)	
Week 16 (n = 300,304,296)	66.8 (61.9 to 71.7)	69.2 (64.6 to 73.7)	64.6 (59.7 to 69.6)	

Week 20 (n = 294,302,295)	69.6 (64.8 to 74.5)	67.3 (62.5 to 72.0)	66.0 (61.2 to 70.7)	
Week 24 (n = 293,306,297)	70.6 (65.7 to 75.6)	69.1 (64.4 to 73.8)	65.5 (60.6 to 70.4)	
Week 28 (n = 284,295,287)	72.0 (67.1 to 76.9)	69.9 (65.2 to 74.5)	67.0 (62.2 to 71.9)	
Week 32 (n = 277,284,280)	72.6 (67.6 to 77.7)	71.9 (67.1 to 76.7)	67.3 (62.4 to 72.2)	
Week 36 (n = 275,281,275)	71.4 (66.3 to 76.4)	69.6 (64.6 to 74.5)	70.1 (65.2 to 75.1)	
Week 40 (n = 275,286,274)	73.8 (68.9 to 78.6)	70.8 (65.9 to 75.6)	70.4 (65.4 to 75.4)	
Week 44 (n = 269,286,272)	73.7 (68.7 to 78.8)	71.1 (66.3 to 75.9)	69.0 (64.0 to 73.9)	
Week 48 (n = 255,286,278)	73.1 (67.8 to 78.3)	73.0 (68.1 to 77.9)	67.1 (62.1 to 72.0)	
Week 52 (n = 267,281,271)	74.5 (69.5 to 79.5)	69.8 (64.8 to 74.8)	71.0 (66.1 to 75.9)	
Week 56 (n = 267,283,261)	74.7 (69.7 to 79.8)	73.4 (68.6 to 78.2)	71.9 (66.8 to 76.9)	
Week 60 (n = 261,277,255)	70.3 (64.9 to 75.7)	67.1 (62.0 to 72.3)	69.4 (64.3 to 74.5)	
Week 64 (n = 258,290,259)	74.5 (69.5 to 79.6)	68.1 (63.0 to 73.2)	68.2 (63.0 to 73.5)	
Week 68 (n = 254,272,255)	71.9 (66.6 to 77.2)	68.4 (63.2 to 73.6)	72.3 (67.2 to 77.4)	
Week 72 (n = 245,261,250)	68.8 (63.2 to 74.3)	72.2 (67.2 to 77.3)	66.2 (60.8 to 71.6)	
Week 76 (n = 257,273,251)	70.1 (64.8 to 75.5)	69.0 (63.9 to 74.2)	70.7 (65.3 to 76.1)	
Week 80 (n = 247,269,250)	72.4 (67.0 to 77.8)	70.9 (65.8 to 76.0)	69.5 (64.0 to 74.9)	
Week 84 (n = 253,265,255)	72.7 (67.4 to 78.0)	71.6 (66.5 to 76.8)	71.4 (66.0 to 76.7)	
Week 88 (n = 254,267,247)	68.7 (63.3 to 74.2)	70.3 (65.1 to 75.5)	71.3 (65.9 to 76.6)	
Week 92 (n = 249,269,242)	71.6 (66.1 to 77.0)	73.5 (68.4 to 78.6)	69.5 (64.0 to 74.9)	
Week 96 (n = 244,267,241)	74.9 (69.5 to 80.3)	73.1 (68.0 to 78.2)	73.2 (67.9 to 78.5)	
Week 100 (n = 251,271,237)	73.5 (68.1 to 78.9)	70.0 (64.8 to 75.1)	76.4 (71.2 to 81.6)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/40 or Better (BCVA ≥69 Letters) in the Study Eye Over Time, Treatment-Naive Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥69 vs. <69 letters) and region (U.S. and Canada vs. rest of the

world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[22]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,243,242)	57.5 (51.9 to 63.1)	59.9 (54.8 to 64.9)	56.0 (50.7 to 61.4)	
Week 8 (n = 244,246,242)	62.3 (56.8 to 67.7)	67.0 (61.9 to 72.1)	59.9 (54.5 to 65.2)	
Week 12 (n = 242,241,236)	68.9 (63.6 to 74.1)	70.2 (65.1 to 75.3)	67.5 (62.1 to 73.0)	
Week 16 (n = 241,241,230)	66.8 (61.3 to 72.3)	70.7 (65.7 to 75.7)	65.0 (59.4 to 70.6)	
Week 20 (n = 233,239,230)	70.2 (64.7 to 75.6)	69.2 (64.0 to 74.3)	67.4 (62.1 to 72.8)	
Week 24 (n = 231,242,232)	71.1 (65.6 to 76.5)	71.7 (66.6 to 76.8)	66.2 (60.8 to 71.7)	
Week 28 (n = 223,232,222)	73.5 (68.1 to 79.0)	71.0 (65.9 to 76.1)	69.4 (64.0 to 74.8)	
Week 32 (n = 216,220,216)	74.3 (68.7 to 80.0)	74.8 (69.4 to 80.1)	70.2 (64.6 to 75.8)	
Week 36 (n = 212,220,209)	71.8 (66.0 to 77.5)	71.2 (65.6 to 76.8)	72.4 (66.9 to 77.9)	
Week 40 (n = 213,222,211)	74.0 (68.6 to 79.5)	73.7 (68.4 to 79.0)	72.3 (66.7 to 77.9)	
Week 44 (n = 208,223,211)	73.8 (68.1 to 79.4)	74.3 (69.1 to 79.6)	73.5 (68.0 to 78.9)	
Week 48 (n = 199,224,212)	73.1 (67.3 to 79.0)	76.2 (70.9 to 81.5)	70.5 (65.0 to 75.9)	
Week 52 (n = 209,223,207)	73.9 (68.2 to 79.5)	73.3 (67.7 to 78.8)	75.5 (70.1 to 80.9)	
Week 56 (n = 209,224,200)	75.9 (70.3 to 81.5)	75.5 (70.3 to 80.7)	74.7 (69.1 to 80.3)	
Week 60 (n = 208,219,200)	69.9 (63.9 to 76.0)	70.9 (65.2 to 76.7)	71.5 (65.8 to 77.2)	
Week 64 (n = 205,228,203)	73.7 (67.9 to 79.4)	70.6 (65.0 to 76.2)	70.4 (64.5 to 76.2)	
Week 68 (n = 201,214,200)	71.8 (65.8 to 77.7)	68.4 (62.5 to 74.3)	73.9 (68.2 to 79.5)	
Week 72 (n = 191,205,196)	67.0 (60.6 to 73.3)	73.9 (68.2 to 79.6)	68.6 (62.6 to 74.6)	
Week 76 (n = 199,216,195)	70.3 (64.1 to 76.4)	72.1 (66.4 to 77.8)	71.7 (65.7 to 77.8)	
Week 80 (n = 189,210,193)	73.2 (67.0 to 79.3)	72.5 (66.8 to 78.3)	72.6 (66.6 to 78.6)	

Week 84 (n = 194,211,191)	73.4 (67.4 to 79.4)	72.2 (66.4 to 78.0)	72.5 (66.6 to 78.5)	
Week 88 (n = 194,211,191)	68.1 (62.0 to 74.3)	70.4 (64.5 to 76.2)	75.3 (69.3 to 81.2)	
Week 92 (n = 192,210,188)	70.5 (64.2 to 76.8)	74.5 (68.6 to 80.4)	73.2 (67.2 to 79.2)	
Week 96 (n = 190,210,189)	72.7 (66.4 to 79.0)	74.8 (69.1 to 80.5)	73.8 (67.9 to 79.8)	
Week 100 (n = 196,213,183)	71.2 (64.9 to 77.4)	70.7 (64.8 to 76.6)	77.7 (71.9 to 83.5)	

Notes:

[22] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA ≤38 Letters) in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA ≤38 Letters) in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point description:

BCVA was measured on the ETDRS chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA from baseline indicates an improvement in visual acuity. For each participant, an average BCVA value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	268	294	279	208
Units: Percentage of participants				
number (confidence interval 95%)	0.8 (0.0 to 1.8)	0.0 (0.0 to 0.0)	0.7 (0.0 to 1.7)	1.0 (0.0 to 2.3)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	232	213		

Units: Percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.5 (0.0 to 1.4)		

Statistical analyses

Statistical analysis title	ITT: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.	
Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.5

Statistical analysis title	ITT: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.	
Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.2

Statistical analysis title	TN: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.	
Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population

Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.1

Statistical analysis title	TN: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.4

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

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA ≤38 Letters) in the Study Eye Over Time, ITT Population

End point description:

Best Corrected Visual Acuity (BCVA) was measured on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at a starting distance of 4 meters. The BCVA letter score ranges from 0 to 100 (best score), and a gain in BCVA letter score from baseline indicates an improvement invisual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 307,308,309)	1.6 (0.2 to 3.0)	1.7 (0.2 to 3.1)	0.3 (0.0 to 1.0)	
Week 8 (n = 306,313,309)	1.3 (0.0 to 2.6)	0.6 (0.0 to 1.5)	0.3 (0.0 to 1.0)	
Week 12 (n = 306,305,302)	1.3 (0.1 to 2.6)	0.7 (0.0 to 1.6)	0.6 (0.0 to 1.5)	
Week 16 (n = 301,306,296)	0.3 (0.0 to 1.0)	0.3 (0.0 to 0.9)	0.7 (0.0 to 1.5)	
Week 20 (n = 294,304,295)	1.0 (0.0 to 2.2)	0.3 (0.0 to 0.9)	1.0 (0.0 to 2.1)	
Week 24 (n = 294,307,297)	0.7 (0.0 to 1.7)	0.3 (0.0 to 1.0)	1.3 (0.1 to 2.6)	
Week 28 (n = 285,295,287)	1.1 (0.0 to 2.2)	0.3 (0.0 to 1.0)	0.7 (0.0 to 1.6)	
Week 32 (n = 278,284,280)	0.7 (0.0 to 1.7)	1.4 (0.1 to 2.8)	1.1 (0.0 to 2.3)	
Week 36 (n = 275,282,275)	0.7 (0.0 to 1.7)	1.3 (0.1 to 2.6)	0.4 (0.0 to 1.0)	
Week 40 (n = 276,287,274)	1.1 (0.0 to 2.4)	1.4 (0.1 to 2.7)	1.1 (0.0 to 2.3)	
Week 44 (n = 270,287,272)	0.4 (0.0 to 1.1)	1.0 (0.0 to 2.2)	1.1 (0.0 to 2.3)	
Week 48 (n = 255,287,278)	0.8 (0.0 to 1.9)	0.7 (0.0 to 1.6)	1.4 (0.1 to 2.7)	
Week 52 (n = 268,282,271)	0.4 (0.0 to 1.2)	0.4 (0.0 to 1.1)	1.1 (0.0 to 2.2)	
Week 56 (n = 268,284,261)	1.1 (0.0 to 2.4)	1.0 (0.0 to 2.2)	0.8 (0.0 to 1.8)	
Week 60 (n = 262,277,255)	1.2 (0.0 to 2.5)	0.7 (0.0 to 1.7)	1.5 (0.1 to 2.9)	
Week 64 (n = 258,291,259)	1.2 (0.0 to 2.4)	0.7 (0.0 to 1.6)	2.0 (0.3 to 3.7)	
Week 68 (n = 255,273,255)	1.2 (0.0 to 2.5)	1.1 (0.0 to 2.4)	0.4 (0.0 to 1.1)	
Week 72 (n = 246,262,250)	1.2 (0.0 to 2.5)	1.9 (0.3 to 3.6)	1.5 (0.1 to 3.0)	
Week 76 (n = 257,274,251)	2.7 (0.8 to 4.7)	1.8 (0.2 to 3.4)	2.0 (0.3 to 3.7)	
Week 80 (n = 248,270,250)	2.4 (0.6 to 4.3)	2.6 (0.7 to 4.6)	1.6 (0.1 to 3.1)	
Week 84 (n = 253,266,255)	2.7 (0.7 to 4.6)	1.2 (0.0 to 2.5)	1.9 (0.3 to 3.5)	
Week 88 (n = 255,268,247)	2.3 (0.5 to 4.1)	1.9 (0.3 to 3.4)	1.2 (0.0 to 2.5)	
Week 92 (n = 250,269,242)	3.2 (1.0 to 5.4)	0.8 (0.0 to 1.8)	1.6 (0.1 to 3.1)	
Week 96 (n = 245,268,241)	2.9 (0.8 to 5.0)	2.3 (0.5 to 4.1)	2.0 (0.3 to 3.7)	
Week 100 (n = 252,272,237)	2.7 (0.7 to 4.7)	3.3 (1.2 to 5.5)	2.5 (0.5 to 4.4)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants with BCVA Snellen Equivalent of 20/200 or Worse (BCVA ≤38 Letters) in the Study Eye Over Time, Treatment-Naive Population

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 attainable), and a gain in BCVA letter score from baseline indicates an improvement in visual acuity. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world were combined). Treatment policy strategy (i.e., all

observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. Invalid BCVA values were excluded from analysis. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[23]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 245,245,242)	2.0 (0.3 to 3.8)	1.7 (0.1 to 3.2)	0.4 (0.0 to 1.2)	
Week 8 (n = 245,248,242)	1.6 (0.1 to 3.2)	0.8 (0.0 to 1.9)	0.4 (0.0 to 1.2)	
Week 12 (n = 243,243,236)	1.2 (0.0 to 2.6)	0.4 (0.0 to 1.2)	0.8 (0.0 to 2.0)	
Week 16 (n = 242,243,230)	0.4 (0.0 to 1.2)	0.4 (0.0 to 1.2)	0.9 (0.0 to 2.0)	
Week 20 (n = 233,241,230)	0.9 (0.0 to 2.1)	0.4 (0.0 to 1.2)	0.9 (0.0 to 2.0)	
Week 24 (n = 232,243,232)	0.9 (0.0 to 2.1)	0.4 (0.0 to 1.2)	0.8 (0.0 to 2.0)	
Week 28 (n = 224,232,222)	1.3 (0.0 to 2.8)	0.4 (0.0 to 1.3)	0.4 (0.0 to 1.3)	
Week 32 (n = 217,220,216)	0.9 (0.0 to 2.2)	1.4 (0.0 to 2.9)	0.5 (0.0 to 1.4)	
Week 36 (n = 212,221,209)	1.0 (0.0 to 2.3)	1.7 (0.1 to 3.4)	0.5 (0.0 to 1.4)	
Week 40 (n = 214,223,211)	1.0 (0.0 to 2.2)	1.8 (0.1 to 3.5)	0.5 (0.0 to 1.4)	
Week 44 (n = 209,224,211)	0.5 (0.0 to 1.4)	1.3 (0.0 to 2.8)	0.5 (0.0 to 1.4)	
Week 48 (n = 199,225,212)	1.0 (0.0 to 2.4)	0.9 (0.0 to 2.1)	0.5 (0.0 to 1.4)	
Week 52 (n = 210,224,207)	0.0 (0.0 to 0.0)	0.5 (0.0 to 1.4)	0.0 (0.0 to 0.0)	
Week 56 (n = 210,225,200)	1.4 (0.0 to 3.0)	0.9 (0.0 to 2.0)	1.0 (0.0 to 2.4)	
Week 60 (n = 209,219,200)	0.9 (0.0 to 2.2)	0.9 (0.0 to 2.2)	1.0 (0.0 to 2.4)	
Week 64 (n = 205,229,203)	0.5 (0.0 to 1.5)	0.9 (0.0 to 2.0)	2.0 (0.1 to 4.0)	
Week 68 (n = 202,215,200)	0.5 (0.0 to 1.5)	1.4 (0.0 to 3.0)	0.5 (0.0 to 1.4)	
Week 72 (n = 192,206,196)	1.0 (0.0 to 2.4)	1.4 (0.0 to 3.1)	2.0 (0.1 to 3.9)	
Week 76 (n = 199,217,195)	2.0 (0.1 to 3.9)	1.8 (0.1 to 3.6)	2.6 (0.4 to 4.7)	
Week 80 (n = 190,211,193)	1.6 (0.0 to 3.4)	2.9 (0.6 to 5.2)	1.5 (0.0 to 3.3)	
Week 84 (n = 194,210,199)	2.1 (0.1 to 4.1)	1.0 (0.0 to 2.3)	2.0 (0.1 to 3.9)	
Week 88 (n = 195,212,191)	1.5 (0.0 to 3.2)	1.9 (0.1 to 3.7)	1.6 (0.0 to 3.3)	
Week 92 (n = 193,210,188)	3.2 (0.7 to 5.6)	0.5 (0.0 to 1.5)	2.1 (0.1 to 4.1)	
Week 96 (n = 191,211,189)	2.7 (0.4 to 5.0)	2.4 (0.3 to 4.5)	2.0 (0.1 to 4.0)	
Week 100 (n = 197,214,183)	3.0 (0.6 to 5.4)	3.8 (1.2 to 6.3)	2.1 (0.1 to 4.1)	

Notes:

[23] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥2-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in

the Study Eye Over Time, ITT Population

End point title	Percentage of Participants with a ≥2-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, ITT Population

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 52, and 96

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 280,289,271)	34.5 (29.1 to 39.8)	38.0 (32.5 to 43.6)	34.0 (28.6 to 39.5)	
Week 52 (n = 249,261,246)	43.4 (37.4 to 49.4)	43.9 (37.9 to 49.8)	46.2 (40.2 to 52.2)	
Week 96 (n = 214,228,203)	53.5 (46.9 to 60.1)	44.3 (37.9 to 50.7)	43.8 (37.2 to 50.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥2-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants with a ≥2-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, Treatment-Naive Population

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a

rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 52, and 96

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[24]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 224,230,209)	37.2 (31.1 to 43.3)	39.5 (33.3 to 45.7)	37.3 (31.0 to 43.7)	
Week 52 (n = 195,206,192)	46.0 (39.1 to 52.9)	46.2 (39.4 to 53.1)	51.3 (44.4 to 58.2)	
Week 96 (n = 161,177,160)	55.2 (47.6 to 62.8)	44.1 (36.9 to 51.4)	48.8 (41.1 to 56.4)	

Notes:

[24] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥3-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants with a ≥3-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, ITT Population

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 52, and 96

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 280,289,271)	12.8 (9.0 to 16.7)	17.0 (12.7 to 21.4)	13.4 (9.3 to 17.4)	
Week 52 (n = 249,261,246)	16.3 (11.7 to 20.8)	19.2 (14.4 to 24.0)	19.2 (14.4 to 24.0)	
Week 96 (n = 214,228,203)	25.1 (19.3 to 30.9)	19.3 (14.2 to 24.5)	21.8 (16.3 to 27.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥3-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants with a ≥3-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, Treatment-Naive Population

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 52, and 96

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[25]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 224,230,209)	14.2 (9.7 to 18.7)	16.6 (11.8 to 21.4)	14.4 (9.6 to 19.1)	
Week 52 (n = 195,206,192)	18.9 (13.4 to 24.4)	19.0 (13.6 to 24.3)	21.6 (15.9 to 27.4)	
Week 96 (n = 161,177,160)	27.9 (21.0 to 34.8)	19.2 (13.4 to 25.0)	25.7 (19.0 to 32.4)	

Notes:

[25] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥4-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants with a ≥4-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, ITT Population

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 52, and 96

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 280,289,271)	3.6 (1.4 to 5.8)	8.3 (5.2 to 11.5)	3.4 (1.2 to 5.5)	
Week 52 (n = 249,261,246)	4.1 (1.6 to 6.5)	7.3 (4.1 to 10.4)	4.9 (2.2 to 7.6)	
Week 96 (n = 214,228,203)	7.7 (4.1 to 11.2)	7.3 (4.0 to 10.6)	5.3 (2.3 to 8.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥4-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in

the Study Eye Over Time, Treatment-Naive Population

End point title	Percentage of Participants with a ≥4-Step Diabetic Retinopathy Severity Improvement From Baseline on the ETDRS Diabetic Retinopathy Severity Scale in the Study Eye Over Time, Treatment-Naive Population

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy. Ocular imaging assessments were made independently by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters) and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 52, and 96

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[26]	248	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 224,230,209)	3.6 (1.1 to 6.0)	6.5 (3.3 to 9.7)	3.3 (0.9 to 5.8)	
Week 52 (n = 195,206,192)	5.1 (2.0 to 8.1)	6.3 (3.0 to 9.7)	4.6 (1.7 to 7.5)	
Week 96 (n = 161,177,160)	9.2 (4.8 to 13.7)	5.6 (2.2 to 9.0)	6.3 (2.5 to 10.0)	

Notes:

[26] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Without Proliferative Diabetic Retinopathy (PDR) at Baseline Who Developed New PDR at Week 52, ITT and Treatment-Naive Populations

End point title	Percentage of Participants Without Proliferative Diabetic Retinopathy (PDR) at Baseline Who Developed New PDR at Week 52, ITT and Treatment-Naive Populations

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced proliferative diabetic retinopathy (PDR). PDR was defined as an ETDRS DRSS score of ≥61 on the 7-field/4-wide field color fundus photographs assessment by a central reading center. The weighted percentages of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% CI is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:
Baseline and Week 52

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	215	221	221	164
Units: Percentage of participants				
number (confidence interval 95%)	0.8 (0.0 to 2.0)	0.9 (0.0 to 2.2)	0.4 (0.0 to 1.3)	0.6 (0.0 to 1.8)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	176	171		
Units: Percentage of participants				
number (confidence interval 95%)	1.2 (0.0 to 2.8)	0.0 (0.0 to 0.0)		

Statistical analyses

Statistical analysis title	ITT: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	436
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.8

Statistical analysis title	ITT: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W

Number of subjects included in analysis	442
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2

Statistical analysis title	TN: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.8

Statistical analysis title	TN: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	347
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	2.8

Secondary: Percentage of Participants Without High-Risk Proliferative Diabetic Retinopathy (PDR) at Baseline Who Developed High-Risk PDR at Week 52, ITT and Treatment-Naive Populations

End point title	Percentage of Participants Without High-Risk Proliferative Diabetic Retinopathy (PDR) at Baseline Who Developed High-Risk PDR at Week 52, ITT and Treatment-Naive Populations

End point description:

The Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) classifies diabetic retinopathy into 12 severity steps ranging from absence of retinopathy to advanced PDR. High-risk PDR was defined as an ETDRS DRSS score of ≥71 on the 7-field/4-wide field color fundus photographs assessment by a central reading center. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% CI is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	230	250	236	178
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	197	182		
Units: Percentage of participants				
number (confidence interval 95%)	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		

Statistical analyses

Statistical analysis title	ITT: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	ITT: Arm B vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	486
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	TN: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.

Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Statistical analysis title	TN: Arm B vs. Arm C

Statistical analysis description:	
This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	379
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Secondary: Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 52, ITT Population

End point title	Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 52, ITT Population[27]

End point description:

The number analyzed includes all participants in the Arm B: Faricimab 6 mg PTI, Intent-to-Treat (ITT) Population who had not discontinued the study prior to Week 52.

End point type	Secondary

End point timeframe:

Week 52

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to participants who were randomized to Arm B: Faricimab 6 mg Personalized Treatment Interval (PTI) and had not discontinued the study prior to Week 52.

End point values	B: Faricimab 6 mg PTI			
Subject group type	Reporting group			
Number of subjects analysed	308			
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 4 Weeks	13.3 (9.5 to 17.1)			
Once Every 8 Weeks	15.6 (11.5 to 19.6)			
Once Every 12 Weeks	20.1 (15.6 to 24.6)			
Once Every 16 Weeks	51.0 (45.4 to 56.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 52, Treatment-Naive Population

End point title	Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 52, Treatment-Naive Population

End point description:

The number analyzed includes all participants in the Arm B: Faricimab 6 mg PTI, Treatment-Naive (TN) Population who had not discontinued the study prior to Week 52.

End point type	Secondary

End point timeframe:

Week 52

End point values	B: Faricimab 6 mg PTI, TN Population			
Subject group type	Subject analysis set			
Number of subjects analysed	245			
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 4 Weeks	11.8 (7.8 to 15.9)			
Once Every 8 Weeks	13.9 (9.5 to 18.2)			
Once Every 12 Weeks	20.0 (15.0 to 25.0)			
Once Every 16 Weeks	54.3 (48.0 to 60.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 96, ITT Population

End point title	Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 96, ITT Population[28]

End point description:

The number analyzed includes all participants in the Arm B: Faricimab 6 mg PTI, Intent-to-Treat (ITT) Population who had not discontinued the study prior to Week 96.

End point type	Secondary

End point timeframe:

Week 96

Notes:

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

Justification: This endpoint is only applicable to participants who were randomized to Arm B: Faricimab 6 mg Personalized Treatment Interval (PTI) and had not discontinued the study prior to Week 96.

End point values	B: Faricimab 6 mg PTI			
Subject group type	Reporting group			
Number of subjects analysed	287			
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 4 Weeks	10.1 (6.6 to 13.6)			
Once Every 8 Weeks	11.8 (8.1 to 15.6)			
Once Every 12 Weeks	13.6 (9.6 to 17.6)			
Once Every 16 Weeks	64.5 (58.9 to 70.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 96, Treatment-Naive Population

End point title	Percentage of Participants in the Faricimab 6 mg PTI Arm on a Once Every 4-Weeks, 8-Weeks, 12-Weeks, or 16-Weeks Treatment Interval at Week 96, Treatment-Naive Population

End point description:

The number analyzed includes all participants in the Arm B: Faricimab 6 mg PTI, Treatment-Naive (TN) Population who had not discontinued the study prior to Week 96.

End point type	Secondary

End point timeframe:

Week 96

End point values	B: Faricimab 6 mg PTI, TN Population			
Subject group type	Subject analysis set			
Number of subjects analysed	227			
Units: Percentage of participants				
number (confidence interval 95%)				
Once Every 4 Weeks	9.3 (5.5 to 13.0)			
Once Every 8 Weeks	9.7 (5.8 to 13.5)			
Once Every 12 Weeks	12.8 (8.4 to 17.1)			

Once Every 16 Weeks	68.3 (62.2 to 74.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in the Faricimab 6 mg PTI Arm at Week 52 who Achieved a Once Every 12-Weeks or 16-Weeks Treatment Interval Without an Interval Decrease Below Once Every 12 Weeks, ITT and Treatment-Naive Populations

End point title	Percentage of Participants in the Faricimab 6 mg PTI Arm at Week 52 who Achieved a Once Every 12-Weeks or 16-Weeks Treatment Interval Without an Interval Decrease Below Once Every 12 Weeks, ITT and Treatment-Naive Populations[29]

End point description:

The number analyzed includes all participants in Arm B: Faricimab 6 mg PTI who had not discontinued the study prior to Week 52.

End point type	Secondary

End point timeframe:

From start of PTI (Week 12 or later) until Week 52

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to participants who were randomized to Arm B: Faricimab 6 mg Personalized Treatment Interval (PTI) and had not discontinued the study prior to Week 52.

End point values	B: Faricimab 6 mg PTI	B: Faricimab 6 mg PTI, TN Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	308	245		
Units: Percentage of participants				
number (confidence interval 95%)	64.3 (58.9 to 69.6)	66.9 (61.0 to 72.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants in the Faricimab 6 mg PTI Arm at Week 96 who Achieved a Once Every 12-Weeks or 16-Weeks Treatment Interval Without an Interval Decrease Below Once Every 12 Weeks, ITT and Treatment-Naive Populations

End point title	Percentage of Participants in the Faricimab 6 mg PTI Arm at Week 96 who Achieved a Once Every 12-Weeks or 16-Weeks Treatment Interval Without an Interval Decrease Below Once Every 12 Weeks, ITT and Treatment-Naive Populations[30]

End point description:

The number analyzed includes all participants in Arm B: Faricimab 6 mg PTI who had not discontinued

the study prior to Week 96.

End point type	Secondary

End point timeframe:

From start of PTI (Week 12 or later) until Week 96

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to participants who were randomized to Arm B: Faricimab 6 mg Personalized Treatment Interval (PTI) and had not discontinued the study prior to Week 96.

End point values	B: Faricimab 6 mg PTI	B: Faricimab 6 mg PTI, TN Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	287	227		
Units: Percentage of participants				
number (confidence interval 95%)	63.1 (57.5 to 68.7)	65.6 (59.4 to 71.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Central Subfield Thickness in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point title	Change From Baseline in Central Subfield Thickness in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by a central reading center. For the Mixed Model for Repeated Measures (MMRM) analysis, the model adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous), baseline BCVA (<64 vs. ≥64 letters), prior intravitreal anti-VEGF therapy (yes vs. no), and region of enrollment (U.S. and Canada vs. the rest of the world; Asia and rest of the world regions were combined). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

From Baseline through Week 56

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	317	319	315	254
Units: microns				
arithmetic mean (confidence interval 95%)	-195.8 (-204.1 to -187.5)	-187.6 (-195.8 to -179.5)	-170.1 (-178.3 to -161.8)	-195.0 (-204.2 to -185.9)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	254	248		
Units: microns				
arithmetic mean (confidence interval 95%)	-189.4 (-198.3 to -180.4)	-175.1 (-184.2 to -165.9)		

Statistical analyses

Statistical analysis title	ITT: Arm A vs. Arm C
Statistical analysis description:	
This is the adjusted mean difference for Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W in the ITT Population.	
Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	632
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted mean difference
Point estimate	-25.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.4
upper limit	-14
Variability estimate	Standard error of the mean
Dispersion value	5.95

Statistical analysis title	ITT: Arm B vs. Arm C
Statistical analysis description:	
This is the adjusted mean difference for Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W in the ITT Population.	
Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	634
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted mean difference
Point estimate	-17.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.2
upper limit	-6

Variability estimate	Standard error of the mean
Dispersion value	5.88

Statistical analysis title	TN: Arm A vs. Arm C
Statistical analysis description:	
This is the adjusted mean difference for Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W in the Treatment-Naive Population.	
Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	502
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted mean difference
Point estimate	-20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.9
upper limit	-7
Variability estimate	Standard error of the mean
Dispersion value	6.59

Statistical analysis title	TN: Arm B vs. Arm C
Statistical analysis description:	
This is the adjusted mean difference for Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W in the Treatment-Naive Population.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	502
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted mean difference
Point estimate	-14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.1
upper limit	-1.5
Variability estimate	Standard error of the mean
Dispersion value	6.51

Secondary: Change From Baseline in Central Subfield Thickness in the Study Eye Over Time, ITT Population

End point title	Change From Baseline in Central Subfield Thickness in the Study Eye Over Time, ITT Population

End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by a central reading center. For the Mixed Model for Repeated Measures (MMRM) analysis, the model adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous), baseline BCVA (<64 vs. ≥64 letters), prior intravitreal anti-VEGF therapy (yes vs. no), and region of enrollment (U.S. and Canada vs. the rest of the world; Asia and rest of the world regions were combined). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: microns				
arithmetic mean (confidence interval 95%)				
Week 4	-106.1 (-115.7 to -96.6)	-113.9 (-123.4 to -104.4)	-107.3 (-116.8 to -97.7)	
Week 8	-132.0 (-140.9 to -123.0)	-139.6 (-148.4 to -130.8)	-129.6 (-138.5 to -120.6)	
Week 12	-146.0 (-154.8 to -137.2)	-155.0 (-163.7 to -146.3)	-143.1 (-151.9 to -134.2)	
Week 16	-162.2 (-170.4 to -154.0)	-167.1 (-175.2 to -158.9)	-151.4 (-159.7 to -143.2)	
Week 20	-166.8 (-176.0 to -157.6)	-157.2 (-166.3 to -148.1)	-154.6 (-163.8 to -145.4)	
Week 24	-179.9 (-188.4 to -171.3)	-181.4 (-189.8 to -173.0)	-146.6 (-155.1 to -138.1)	
Week 28	-164.8 (-173.2 to -156.5)	-184.0 (-192.3 to -175.8)	-165.0 (-173.3 to -156.6)	
Week 32	-181.9 (-191.4 to -172.4)	-169.4 (-178.9 to -160.0)	-154.8 (-164.3 to -145.3)	
Week 36	-170.9 (-179.8 to -162.1)	-189.2 (-197.9 to -180.5)	-168.6 (-177.4 to -159.7)	
Week 40	-191.6 (-200.9 to -182.3)	-183.8 (-193.0 to -174.6)	-160.0 (-169.3 to -150.7)	
Week 44	-181.7 (-191.0 to -172.3)	-185.9 (-195.1 to -176.7)	-172.3 (-181.7 to -162.9)	
Week 48	-195.6 (-205.0 to -186.2)	-184.9 (-194.1 to -175.8)	-162.7 (-172.0 to -153.4)	
Week 52	-188.6 (-197.9 to -179.3)	-186.1 (-195.3 to -177.0)	-176.6 (-185.9 to -167.3)	
Week 56	-199.0 (-208.4 to -189.7)	-188.5 (-197.7 to -179.4)	-168.2 (-177.5 to -158.8)	
Week 60	-194.1 (-204.1 to -184.0)	-186.1 (-195.9 to -176.3)	-179.0 (-189.1 to -168.9)	
Week 64	-197.2 (-206.7 to -187.8)	-189.8 (-199.0 to -180.7)	-172.1 (-181.5 to -162.8)	
Week 68	-196.2 (-205.2 to -187.1)	-190.3 (-199.2 to -181.5)	-181.4 (-190.4 to -172.4)	

Week 72	-202.8 (-212.3 to -193.4)	-191.9 (-201.2 to -182.6)	-172.5 (-181.9 to -163.0)	
Week 76	-198.8 (-207.4 to -190.3)	-191.3 (-199.6 to -182.9)	-185.4 (-194.0 to -176.8)	
Week 80	-204.0 (-213.4 to -194.6)	-189.7 (-198.8 to -180.5)	-176.7 (-186.1 to -167.3)	
Week 84	-198.2 (-207.6 to -188.9)	-197.9 (-207.1 to -188.8)	-185.5 (-194.7 to -176.2)	
Week 88	-201.5 (-211.3 to -191.7)	-194.9 (-204.4 to -185.3)	-177.1 (-186.9 to -167.3)	
Week 92	-200.5 (-210.2 to -190.9)	-195.4 (-204.7 to -186.1)	-184.0 (-193.7 to -174.4)	
Week 96	-206.3 (-215.7 to -196.8)	-199.0 (-208.2 to -189.7)	-180.0 (-189.5 to -170.5)	
Week 100	-201.1 (-210.5 to -191.8)	-196.9 (-206.0 to -187.8)	-192.8 (-202.2 to -183.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Central Subfield Thickness in the Study Eye Over Time, Treatment-Naive Population

End point title	Change From Baseline in Central Subfield Thickness in the Study Eye Over Time, Treatment-Naive Population

End point description:

Central subfield thickness (CST) was defined as the distance between the internal limiting membrane (ILM) and Bruch's membrane (BM) as assessed by a central reading center. For the Mixed Model for Repeated Measures (MMRM) analysis, the model adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous), baseline BCVA (<64 vs. ≥64 letters), and region of enrollment (U.S. and Canada vs. the rest of the world; Asia and rest of the world regions were combined). An unstructured covariance structure was used. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W, TN Population	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	254	254[31]	248	
Units: microns				
arithmetic mean (confidence interval 95%)				
Week 4	-106.3 (-116.9 to -95.6)	-112.9 (-123.5 to -102.3)	-106.3 (-117.0 to -95.6)	
Week 8	-131.8 (-141.6 to -122.0)	-140.6 (-150.3 to -130.9)	-130.4 (-140.2 to -120.5)	

Week 12	-148.8 (-158.4 to -139.2)	-156.6 (-166.2 to -147.1)	-145.3 (-154.9 to -135.6)	
Week 16	-163.0 (-171.9 to -154.0)	-168.8 (-177.7 to -159.9)	-157.0 (-166.0 to -148.0)	
Week 20	-170.5 (-180.1 to -160.9)	-162.3 (-171.9 to -152.8)	-160.6 (-170.2 to -150.9)	
Week 24	-182.4 (-191.5 to -173.3)	-182.9 (-191.9 to -173.9)	-154.6 (-163.8 to -145.5)	
Week 28	-166.8 (-175.9 to -157.8)	-183.9 (-192.0 to -174.9)	-174.2 (-183.2 to -165.1)	
Week 32	-183.7 (-194.0 to -173.4)	-168.0 (-178.2 to -157.7)	-161.0 (-171.4 to -150.7)	
Week 36	-173.8 (-183.5 to -164.1)	-191.5 (-201.1 to -182.0)	-175.6 (-185.2 to -165.9)	
Week 40	-191.6 (-201.9 to -181.4)	-186.9 (-197.0 to -176.8)	-165.6 (-175.8 to -155.3)	
Week 44	-181.4 (-191.7 to -171.1)	-188.9 (-199.1 to -178.8)	-177.6 (-187.9 to -167.3)	
Week 48	-194.5 (-205.1 to -184.0)	-186.8 (-197.1 to -176.6)	-165.8 (-176.3 to -155.4)	
Week 52	-188.7 (-198.8 to -178.7)	-186.6 (-196.5 to -176.8)	-181.3 (-191.4 to -171.3)	
Week 56	-196.7 (-207.0 to -186.4)	-189.9 (-200.0 to -179.8)	-174.0 (-184.3 to -163.6)	
Week 60	-194.3 (-205.6 to -183.0)	-185.2 (-196.3 to -174.1)	-184.1 (-195.5 to -172.7)	
Week 64	-196.5 (-207.3 to -185.6)	-191.2 (-201.7 to -180.7)	-175.6 (-186.5 to -164.8)	
Week 68	-194.6 (-204.4 to -184.8)	-192.7 (-202.3 to -183.1)	-186.3 (-196.1 to -176.5)	
Week 72	-200.9 (-211.0 to -190.8)	-193.4 (-203.3 to -183.5)	-178.0 (-188.1 to -167.9)	
Week 76	-200.2 (-209.6 to -190.8)	-192.0 (-201.2 to -182.9)	-190.2 (-199.7 to -180.8)	
Week 80	-202.6 (-212.9 to -192.4)	-190.0 (-199.9 to -180.1)	-182.6 (-192.8 to -172.4)	
Week 84	-199.3 (-209.8 to -188.7)	-196.0 (-206.3 to -185.8)	-189.5 (-200.0 to -179.0)	
Week 88	-200.3 (-211.3 to -189.4)	-195.6 (-206.2 to -184.9)	-181.9 (-192.8 to -170.9)	
Week 92	-199.3 (-209.9 to -188.7)	-196.0 (-206.3 to -185.8)	-187.2 (-197.8 to -176.6)	
Week 96	-204.5 (-215.1 to -193.8)	-200.8 (-211.1 to -190.4)	-182.9 (-193.5 to -172.2)	
Week 100	-200.9 (-211.1 to -190.6)	-198.7 (-208.6 to -188.8)	-193.5 (-203.8 to -183.2)	

Notes:

[31] - One subject was excluded from the TN Population due to a late report of prior anti-VEGF treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Absence of Diabetic Macular Edema in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point title	Percentage of Participants with Absence of Diabetic Macular Edema in the Study Eye Averaged Over Weeks 48, 52, and 56, ITT and Treatment-Naive Populations

End point description:

Absence of diabetic macular edema was defined as achieving a central subfield thickness (CST) of <325 microns in the study eye. CST was defined as the distance between the internal limiting membrane and Bruch's membrane. For each participant, an average CST value was calculated across the three visits, and this averaged value was then used to determine if the endpoint was met. The results were summarized as the percentage of participants per treatment arm who met the endpoint. The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world). Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Average of Weeks 48, 52, and 56

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	A: Faricimab 6 mg Q8W, TN Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	268	294	279	208
Units: Percentage of participants				
number (confidence interval 95%)	85.5 (81.3 to 89.7)	81.5 (77.1 to 85.9)	73.2 (68.0 to 78.3)	86.0 (81.3 to 90.7)

End point values	B: Faricimab 6 mg PTI, TN Population	C: Aflibercept 2 mg Q8W, TN Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	232	213		
Units: Percentage of participants				
number (confidence interval 95%)	83.2 (78.4 to 88.0)	77.0 (71.3 to 82.6)		

Statistical analyses

Statistical analysis title	ITT: Arm A vs. Arm C

Statistical analysis description:

This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.

Comparison groups	A: Faricimab 6 mg Q8W v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	547
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	12.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.7
upper limit	18.9

Statistical analysis title	ITT: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the ITT Population.	
Comparison groups	B: Faricimab 6 mg PTI v C: Aflibercept 2 mg Q8W
Number of subjects included in analysis	573
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	14.9

Statistical analysis title	TN: Arm A vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants in Arm A: Faricimab 6 mg Q8W minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.	
Comparison groups	A: Faricimab 6 mg Q8W, TN Population v C: Aflibercept 2 mg Q8W, TN Population
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	16.3

Statistical analysis title	TN: Arm B vs. Arm C
Statistical analysis description:	
This is the difference in percentage of participants in Arm B: Faricimab 6 mg PTI minus Arm C: Aflibercept 2 mg Q8W for the Treatment-Naive Population.	
Comparison groups	B: Faricimab 6 mg PTI, TN Population v C: Aflibercept 2 mg Q8W, TN Population

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in CMH Weighted Percentage
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	13.6

Secondary: Percentage of Participants with Absence of Diabetic Macular Edema in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants with Absence of Diabetic Macular Edema in the Study Eye Over Time, ITT Population

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 estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 309,308,308)	38.2 (32.8 to 43.6)	43.5 (38.0 to 49.0)	38.1 (32.8 to 43.5)	
Week 8 (n = 304,312,307)	53.3 (47.7 to 58.9)	57.3 (51.9 to 62.7)	47.9 (42.4 to 53.5)	
Week 12 (n = 306,304,302)	61.8 (56.5 to 67.2)	64.8 (59.4 to 70.1)	56.4 (50.8 to 62.0)	
Week 16 (n = 296,304,294)	69.2 (64.0 to 74.4)	69.1 (63.9 to 74.2)	62.3 (56.8 to 67.8)	
Week 20 (n = 294,298,294)	73.8 (68.9 to 78.8)	67.2 (62.0 to 72.4)	67.4 (62.1 to 72.7)	
Week 24 (n = 291,302,298)	77.7 (73.0 to 82.4)	77.9 (73.2 to 82.5)	62.4 (57.0 to 67.9)	
Week 28 (n = 280,292,286)	72.1 (67.0 to 77.3)	81.2 (76.8 to 85.6)	71.2 (66.1 to 76.4)	

Week 32 (n = 277,279,280)	80.2 (75.6 to 84.9)	72.1 (67.0 to 77.3)	67.0 (61.5 to 72.4)	
Week 36 (n = 271,279,276)	73.8 (68.7 to 79.0)	83.8 (79.5 to 88.1)	74.6 (69.6 to 79.7)	
Week 40 (n = 273,281,275)	86.1 (82.1 to 90.2)	81.5 (77.0 to 86.0)	72.1 (66.9 to 77.3)	
Week 44 (n = 269,281,270)	81.5 (76.9 to 86.0)	80.3 (75.7 to 84.9)	76.6 (71.6 to 81.6)	
Week 48 (n = 247,281,272)	87.5 (83.4 to 91.6)	82.7 (78.4 to 87.1)	71.0 (65.7 to 76.4)	
Week 52 (n = 266,279,271)	83.7 (79.3 to 88.2)	82.1 (77.6 to 86.6)	76.4 (71.5 to 81.4)	
Week 56 (n = 263,284,261)	89.5 (85.9 to 93.2)	85.4 (81.4 to 89.5)	72.2 (66.9 to 77.6)	
Week 60 (n = 258,273,253)	85.4 (81.1 to 89.6)	86.1 (82.0 to 90.1)	78.8 (73.9 to 83.8)	
Week 64 (n = 249,288,258)	87.6 (83.5 to 91.7)	82.8 (78.5 to 87.2)	73.8 (68.5 to 79.0)	
Week 68 (n = 252,268,254)	85.0 (80.6 to 89.3)	83.2 (78.8 to 87.6)	78.2 (73.1 to 83.2)	
Week 72 (n = 244,260,248)	88.9 (85.1 to 92.8)	82.4 (77.8 to 86.9)	74.6 (69.2 to 80.0)	
Week 76 (n = 247,266,247)	88.4 (84.6 to 92.3)	82.2 (77.7 to 86.7)	79.3 (74.3 to 84.4)	
Week 80 (n = 243,265,244)	90.0 (86.3 to 93.8)	83.4 (78.9 to 87.8)	76.6 (71.4 to 81.9)	
Week 84 (n = 246,261,251)	88.2 (84.2 to 92.2)	85.8 (81.6 to 90.0)	80.3 (75.4 to 85.2)	
Week 88 (n = 248,263,245)	89.5 (85.9 to 93.2)	85.0 (80.7 to 89.2)	78.8 (73.8 to 83.9)	
Week 92 (n = 246,266,242)	88.4 (84.5 to 92.4)	84.6 (80.3 to 88.9)	80.3 (75.3 to 85.3)	
Week 96 (n = 243,263,239)	92.7 (89.5 to 95.8)	88.1 (84.2 to 92.0)	80.0 (74.9 to 85.0)	
Week 100 (n = 245,267,233)	90.6 (87.0 to 94.2)	85.5 (81.3 to 89.7)	84.2 (79.6 to 88.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Retinal Dryness in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants with Retinal Dryness in the Study Eye Over Time, ITT Population

End point description:

Retinal dryness was defined as achieving a central subfield thickness (ILM-BM) of <280 microns. 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 estimates of the percentage of participants was based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world; Asia and rest of the world regions were combined). Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

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

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 4 (n = 309,308,308)	12.3 (8.7 to 16.0)	18.5 (14.2 to 22.8)	15.0 (11.0 to 18.9)	
Week 8 (n = 304,312,307)	26.2 (21.3 to 31.0)	25.9 (21.1 to 30.8)	22.5 (17.9 to 27.2)	
Week 12 (n = 306,304,302)	33.1 (27.9 to 38.3)	36.7 (31.3 to 42.0)	28.2 (23.2 to 33.3)	
Week 16 (n = 296,304,294)	38.5 (33.1 to 44.0)	45.0 (39.4 to 50.5)	33.4 (28.0 to 38.8)	
Week 20 (n = 294,298,294)	44.3 (38.7 to 49.9)	41.0 (35.5 to 46.5)	38.5 (32.9 to 44.0)	
Week 24 (n = 291,302,298)	50.2 (44.6 to 55.8)	52.3 (46.8 to 57.9)	37.0 (31.5 to 42.4)	
Week 28 (n = 280,292,286)	45.2 (39.5 to 50.8)	51.9 (46.4 to 57.3)	46.0 (40.3 to 51.8)	
Week 32 (n = 277,279,280)	52.3 (46.6 to 58.1)	46.6 (41.0 to 52.3)	42.7 (36.9 to 48.4)	
Week 36 (n = 271,279,276)	50.0 (44.2 to 55.7)	59.6 (54.0 to 65.1)	48.8 (42.9 to 54.6)	
Week 40 (n = 273,281,275)	61.2 (55.5 to 66.8)	57.7 (52.0 to 63.3)	49.4 (43.6 to 55.2)	
Week 44 (n = 269,281,270)	59.9 (54.3 to 65.5)	58.6 (53.0 to 64.1)	53.5 (47.7 to 59.4)	
Week 48 (n = 247,281,272)	67.5 (61.7 to 73.2)	58.3 (52.8 to 63.8)	50.2 (44.3 to 56.1)	
Week 52 (n = 266,279,271)	64.5 (58.8 to 70.1)	60.9 (55.3 to 66.4)	54.2 (48.4 to 60.1)	
Week 56 (n = 263,284,261)	70.3 (64.9 to 75.6)	63.6 (58.2 to 69.1)	51.2 (45.2 to 57.1)	
Week 60 (n = 258,273,253)	65.4 (59.8 to 71.1)	65.7 (60.1 to 71.2)	59.2 (53.3 to 65.2)	
Week 64 (n = 249,288,258)	71.6 (66.2 to 77.1)	58.7 (53.1 to 64.2)	52.8 (46.8 to 58.7)	
Week 68 (n = 252,268,254)	66.9 (61.2 to 72.6)	60.6 (55.0 to 66.2)	59.8 (53.9 to 65.8)	
Week 72 (n = 244,260,248)	71.2 (65.6 to 76.7)	65.6 (60.1 to 71.1)	58.8 (52.8 to 64.8)	
Week 76 (n = 247,266,247)	68.4 (62.9 to 74.0)	62.8 (57.2 to 68.5)	58.9 (52.9 to 64.9)	
Week 80 (n = 243,265,244)	72.6 (67.2 to 78.1)	64.0 (58.4 to 69.7)	60.1 (54.1 to 66.1)	
Week 84 (n = 246,261,251)	68.4 (62.8 to 74.0)	67.6 (62.1 to 73.1)	60.7 (54.7 to 66.6)	
Week 88 (n = 248,263,245)	71.8 (66.4 to 77.2)	63.3 (57.7 to 68.9)	60.3 (54.2 to 66.4)	
Week 92 (n = 246,266,242)	72.9 (67.5 to 78.3)	64.6 (59.0 to 70.2)	64.0 (58.0 to 70.1)	

Week 96 (n = 243,263,239)	75.1 (69.9 to 80.3)	67.4 (62.0 to 72.9)	63.1 (57.0 to 69.1)	
Week 100 (n = 245,267,233)	72.0 (66.6 to 77.4)	69.3 (63.9 to 74.6)	64.8 (58.8 to 70.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants with Absence of Intraretinal Fluid in the Study Eye Over Time, ITT Population

End point description:

Intraretinal fluid was measured using optical coherence tomography (OCT) in the central subfield (center 1 mm). The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world); Asia and rest of the world regions were combined due to a small number of enrolled participants. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, 52, 56, 92, 96, and 100

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 296,303,294)	19.6 (15.1 to 24.1)	19.8 (15.4 to 24.2)	13.3 (9.4 to 17.1)	
Week 48 (n = 246,276,269)	40.9 (34.8 to 47.0)	32.3 (26.9 to 37.7)	22.5 (17.6 to 27.3)	
Week 52 (n = 262,280,269)	39.1 (33.3 to 44.9)	35.9 (30.3 to 41.5)	28.4 (23.1 to 33.7)	
Week 56 (n = 260,277,258)	42.5 (36.6 to 48.3)	39.9 (34.2 to 45.6)	27.3 (22.0 to 32.7)	
Week 92 (n = 240,259,234)	56.0 (49.8 to 62.2)	45.0 (39.0 to 51.0)	39.2 (33.0 to 45.4)	
Week 96 (n = 239,256,231)	62.3 (56.3 to 68.4)	47.6 (41.5 to 53.6)	39.1 (32.8 to 45.3)	
Week 100 (n = 238,261,229)	56.6 (50.4 to 62.8)	52.2 (46.2 to 58.1)	45.1 (38.7 to 51.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Absence of Subretinal Fluid in the Study Eye Over Time, ITT Population

End point title	Percentage of Participants with Absence of Subretinal Fluid in the Study Eye Over Time, ITT Population

End point description:

Subretinal fluid was measured using optical coherence tomography (OCT) in the central subfield (center 1 mm). The weighted estimates of the percentage of participants were based on the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world); Asia and rest of the world regions were combined due to a small number of enrolled participants. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, 52, 56, 92, 96, and 100

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 294,305,293)	99.0 (97.9 to 100.0)	96.7 (94.7 to 98.7)	95.6 (93.3 to 97.8)	
Week 48 (n = 251,280,272)	97.2 (95.1 to 99.2)	95.8 (93.5 to 98.1)	95.3 (92.8 to 97.8)	
Week 52 (n = 267,281,271)	94.7 (91.9 to 97.4)	95.7 (93.4 to 98.0)	97.8 (96.1 to 99.5)	
Week 56 (n = 266,283,263)	97.0 (95.0 to 99.0)	95.8 (93.5 to 98.1)	95.9 (93.5 to 98.2)	
Week 92 (n = 245,264,241)	95.0 (92.3 to 97.8)	96.2 (93.9 to 98.5)	96.0 (93.5 to 98.4)	
Week 96 (n = 244,263,238)	96.3 (94.0 to 98.7)	96.6 (94.5 to 98.8)	96.2 (93.8 to 98.6)	
Week 100 (n = 247,266,233)	96.0 (93.5 to 98.4)	96.2 (93.9 to 98.5)	95.9 (93.5 to 98.3)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants with Absence of Intraretinal Fluid and Subretinal Fluid in the Study Eye Over Time, ITT Population

End point description:

Intraretinal fluid and subretinal fluid were measured using optical coherence tomography (OCT) in the central subfield (center 1 mm). The weighted estimates of the percentage of participants were based on

the Cochran-Mantel Haenszel (CMH) weights stratified by baseline BCVA (≥64 vs. <64 letters), prior IVT anti-VEGF therapy (yes vs. no), and region (U.S. and Canada vs. rest of the world); Asia and rest of the world regions were combined due to a small number of enrolled participants. Treatment policy strategy (i.e., all observed values used) and hypothetical strategy (i.e., all values censored after the occurrence of the intercurrent event) were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were not imputed. 95% confidence interval (CI) is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 16, 48, 52, 56, 92, 96, and 100

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: Percentage of participants				
number (confidence interval 95%)				
Week 16 (n = 296,303,294)	19.6 (15.1 to 24.1)	19.1 (14.8 to 23.5)	13.3 (9.4 to 17.1)	
Week 48 (n = 246,276,269)	40.5 (34.4 to 46.6)	31.2 (25.8 to 36.6)	22.5 (17.6 to 27.3)	
Week 52 (n = 262,279,269)	39.1 (33.3 to 44.9)	34.9 (29.4 to 40.5)	28.4 (23.1 to 33.7)	
Week 56 (n = 261,277,258)	42.3 (36.4 to 48.2)	39.2 (33.5 to 44.9)	26.6 (21.3 to 31.8)	
Week 92 (n = 240,259,234)	55.2 (49.0 to 61.4)	44.2 (38.2 to 50.2)	38.3 (32.2 to 44.5)	
Week 96 (n = 239,256,231)	61.0 (54.9 to 67.2)	46.5 (40.4 to 52.5)	38.2 (32.0 to 44.4)	
Week 100 (n = 238,262,228)	54.9 (48.7 to 61.2)	51.2 (45.2 to 57.2)	44.8 (38.4 to 51.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the National Eye Institute Visual Functioning Questionnaire–25 (NEI VFQ-25) Composite Score Over Time, ITT Population

End point title	Change From Baseline in the National Eye Institute Visual Functioning Questionnaire–25 (NEI VFQ-25) Composite Score Over Time, ITT Population

End point description:

The NEI VFQ-25 captures a patient's perception of vision-related functioning and quality of life. The core measure includes 25 items that comprise 11 vision-related subscales and one item on general health. The composite score ranges from 0 to 100, with higher scores, or a positive change from baseline, indicating better vision-related functioning. For the Mixed Model for Repeated Measures (MMRM) analysis, the model adjusted for treatment arm, visit, visit-by-treatment arm interaction, baseline NEI VFQ-25 Composite Score (continuous), baseline BCVA (<64 vs. ≥64 letters), prior intravitreal anti-VEGF therapy (yes vs. no), and region of enrollment. An unstructured covariance structure was used. Treatment policy strategy and hypothetical strategy were applied to non-COVID-19 related and COVID-19 related intercurrent events, respectively. Missing data were implicitly imputed by MMRM. 95% CI is a rounding of 95.04% CI.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 52, and 100

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	315	
Units: score on a scale				
arithmetic mean (confidence interval 95%)				
Week 24	5.7 (4.6 to 6.9)	6.5 (5.4 to 7.7)	7.0 (5.9 to 8.1)	
Week 52	6.8 (5.5 to 8.2)	6.6 (5.3 to 7.9)	7.6 (6.3 to 9.0)	
Week 100	8.8 (7.3 to 10.3)	7.3 (5.9 to 8.7)	6.9 (5.4 to 8.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with at Least One Adverse Event

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

End point description:

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

End point type	Secondary

End point timeframe:

From first dose of study drug through end of study (up to 2 years)

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	314	
Units: Percentage of participants				
number (not applicable)				
Adverse Event (AE)	89.3	85.3	87.3	
Serious AE (SAE)	30.6	25.7	31.8	
AE Leading to Withdrawal from Study Treatment	2.2	2.8	1.6	
AE of Special Interest (AESI)	7.6	7.2	6.4	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

This analysis of adverse events (AEs) only includes ocular AEs, which are categorized as having occurred either in the study eye or 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:

From first dose of study drug through end of study (up to 2 years)

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	314	
Units: Percentage of participants				
number (not applicable)				
Study Eye: Adverse Event (AE)	52.4	51.7	44.6	
Study Eye: Serious AE (SAE)	4.4	6.3	4.1	
Study Eye: AE Leading to Withdrawal from Treatment	0.3	1.9	0.3	
Study Eye: Treatment-related AE	3.2	4.4	4.8	
Study Eye: Treatment-related SAE	0.0	0.9	0.0	
Study Eye: AE of Special Interest (AESI)	4.4	6.3	3.8	
Study Eye: AESI, Drop in VA Score ≥30 Letters	3.2	5.0	2.9	
Study Eye: AESI, Associated with Severe IOI	0.3	0.0	0.3	
StudyEye:AESI,Interv Req to Avoid Perm Vision Loss	0.9	1.3	1.0	
Fellow Eye: AE	50.5	43.3	44.3	
Fellow Eye: SAE	3.5	1.9	3.5	
Fellow Eye: AESI	3.8	0.9	2.9	
Fellow Eye: AESI, Drop in VA Score ≥30 Letters	3.5	0.6	2.5	
Fellow Eye: AESI, Associated with Severe IOI	0.0	0.0	0.0	

FellowEye:AESI,Inter Req to Avoid Perm Vision Loss	0.3	0.3	0.3	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

This analysis of adverse events (AEs) 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:

From first dose of study drug through end of study (up to 2 years)

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	317	319	314	
Units: Percentage of participants				
number (not applicable)				
Adverse Event (AE)	69.4	68.3	73.6	
Serious AE (SAE)	24.0	20.1	28.3	
AE Leading to Withdrawal from Study Treatment	1.9	0.9	1.3	
AE of Special Interest (AESI)	0.0	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[32]

End point description:

Faricimab concentration in plasma was determined using a validated immunoassay method.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 (Baseline); Weeks 4, 28, 52, 76, and 100

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to participants in Arms A and B who received treatment with faricimab and had at least one plasma sample, provided sufficient dosing information (dose and dosing time) was available.

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	315	319		
Units: micrograms per millilitre (µg/mL)				
arithmetic mean (standard deviation)				
Baseline (n = 298, 305)	0.0001 (± 0.0020)	0.0000 (± 0.0004)		
Week 4 (n = 284, 287)	0.0192 (± 0.0163)	0.0196 (± 0.0151)		
Week 28 (n = 266, 283)	0.0030 (± 0.0050)	0.0115 (± 0.0189)		
Week 52 (n = 248, 270)	0.0042 (± 0.0078)	0.0113 (± 0.0140)		
Week 76 (n = 237, 250)	0.0060 (± 0.0093)	0.0060 (± 0.0103)		
Week 100 (n = 254, 267)	0.0058 (± 0.0106)	0.0071 (± 0.0110)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants who Test Positive for Treatment-Emergent Anti-Drug Antibodies Against Faricimab During the Study[33]

End point description:

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

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 28, 52, 76, and 100

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to participants in Arms A and B who received treatment with faricimab and had at least one determinant post-baseline ADA assessment.

End point values	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313	318		
Units: Percentage of participants				
number (not applicable)				
Total Treatment-Emergent ADA-Positive	7.0	8.2		
Treatment-Induced ADA-Positive	7.0	8.2		
Treatment-Boosted ADA-Positive	0.0	0.0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline until Week 100

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	A: Faricimab 6 mg Q8W

Reporting group description:

Participants randomized to Arm A received 6 milligrams (mg) faricimab intravitreal (IVT) injections once every 4 weeks (Q4W) to Week 20, followed by 6 mg faricimab IVT injections once every 8 weeks (Q8W) to Week 96, followed by the final study visit at Week 100.

Reporting group title	B: Faricimab 6 mg PTI

Reporting group description:

Participants randomized to Arm B received 6 milligrams (mg) faricimab intravitreal (IVT) injections Q4W to at least Week 12, followed by a personalized treatment interval (PTI) dosing of 6 mg faricimab IVT injections up to once every 16 weeks (Q16W) through Week 96, followed by the final study visit at Week 100.

Reporting group title	C: Aflibercept 2 mg Q8W

Reporting group description:

Participants randomized to Arm C received 2 milligrams (mg) aflibercept intravitreal (IVT) injections Q4W to Week 16, followed by 2 mg aflibercept IVT injections Q8W to Week 96, followed by the final study visit at Week 100.

Serious adverse events	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W
Total subjects affected by serious adverse events			
subjects affected / exposed	97 / 317 (30.60%)	82 / 319 (25.71%)	100 / 314 (31.85%)
number of deaths (all causes)	12	9	10
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			

subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Hairy cell leukaemia			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma stage II			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer metastatic			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pancreatic neoplasm			

subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extremity necrosis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	2 / 317 (0.63%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 urgency			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 317 (0.00%)	2 / 319 (0.63%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Orthostatic hypotension			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral vascular disorder			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Haematoma			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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			
Haemodialysis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hospitalisation			

subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Necrosis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Pyrexia			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue inflammation			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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

Asthenia			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Death			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Generalised oedema			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Hernia obstructive			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Peripheral swelling			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Hypersensitivity			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 317 (0.63%)	2 / 319 (0.63%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dyspnoea			
subjects affected / exposed	2 / 317 (0.63%)	4 / 319 (1.25%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lung disorder			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Pleural effusion			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 fibrosis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 oedema			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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 failure			
subjects affected / exposed	2 / 317 (0.63%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Depression			

subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Anxiety			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Suicide attempt			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Investigations			
Blood glucose fluctuation			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Intraocular pressure increased			
subjects affected / exposed	2 / 317 (0.63%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biopsy bladder			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Chemical burns of eye			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corneal abrasion			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 317 (0.00%)	2 / 319 (0.63%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture displacement			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Limb injury			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nail avulsion			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			

subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Ankle fracture			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative ileus			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Rib fracture			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Tibia fracture			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Upper limb fracture			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
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 coronary syndrome			

subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 myocardial infarction			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Angina pectoris			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 317 (0.32%)	2 / 319 (0.63%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 317 (0.32%)	2 / 319 (0.63%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 317 (0.63%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Cardiac failure			

subjects affected / exposed	2 / 317 (0.63%)	3 / 319 (0.94%)	4 / 314 (1.27%)
occurrences causally related to treatment / all	0 / 2	0 / 4	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
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 chronic			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Cardiac failure congestive			
subjects affected / exposed	8 / 317 (2.52%)	4 / 319 (1.25%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 10	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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	5 / 317 (1.58%)	3 / 319 (0.94%)	4 / 314 (1.27%)
occurrences causally related to treatment / all	0 / 5	1 / 3	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Myocardial ischaemia			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			

subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Subendocardial ischaemia			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Chronic left ventricular failure			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 heart disease			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral infarction			

subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	4 / 314 (1.27%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical radiculopathy			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Lacunar stroke			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 cord compression			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	2 / 317 (0.63%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lacunar infarction			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Leukoencephalopathy			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Monoplegia			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Status epilepticus			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 317 (0.32%)	2 / 319 (0.63%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Microcytic anaemia			

subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy mediastinal			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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			
Cataract			
subjects affected / exposed	4 / 317 (1.26%)	7 / 319 (2.19%)	7 / 314 (2.23%)
occurrences causally related to treatment / all	0 / 5	1 / 7	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract subcapsular			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic retinal oedema			
subjects affected / exposed	7 / 317 (2.21%)	2 / 319 (0.63%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 10	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic retinopathy			
subjects affected / exposed	0 / 317 (0.00%)	2 / 319 (0.63%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dry eye			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Eye haemorrhage			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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 fibrosis			

subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal tear			
subjects affected / exposed	0 / 317 (0.00%)	2 / 319 (0.63%)	0 / 314 (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
Retinal vein occlusion			
subjects affected / exposed	0 / 317 (0.00%)	2 / 319 (0.63%)	0 / 314 (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
Visual acuity reduced			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual impairment			
subjects affected / exposed	0 / 317 (0.00%)	2 / 319 (0.63%)	0 / 314 (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
Vitreous haemorrhage			
subjects affected / exposed	4 / 317 (1.26%)	1 / 319 (0.31%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angle closure glaucoma			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Cataract nuclear			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic eye disease			

subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Iridocyclitis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open angle glaucoma			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Posterior capsule opacification			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Retinal artery occlusion			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal degeneration			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Vitreous detachment			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Gastrointestinal disorders			
Colitis			

subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
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 dysplasia			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
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 haemorrhage			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Anorectal varices			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haematoma			

subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
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			
Bile duct stenosis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 317 (0.00%)	2 / 319 (0.63%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 317 (1.26%)	4 / 319 (1.25%)	4 / 314 (1.27%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Azotaemia			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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

Calculus urinary			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	4 / 317 (1.26%)	0 / 319 (0.00%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Diabetic nephropathy			
subjects affected / exposed	2 / 317 (0.63%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	3 / 317 (0.95%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Renal failure			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract inflammation			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
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 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			

subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Renal impairment			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Endocrine disorders			
Hyperplasia adrenal			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
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			
Neuropathic arthropathy			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylitis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Pain in extremity			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Rotator cuff syndrome			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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

Arthritis bacterial			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	3 / 317 (0.95%)	1 / 319 (0.31%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cellulitis			
subjects affected / exposed	3 / 317 (0.95%)	1 / 319 (0.31%)	8 / 314 (2.55%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis gangrenous			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Cystitis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot infection			
subjects affected / exposed	4 / 317 (1.26%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic gangrene			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			

subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	2 / 317 (0.63%)	1 / 319 (0.31%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder empyema			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	2 / 317 (0.63%)	2 / 319 (0.63%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Osteomyelitis			
subjects affected / exposed	2 / 317 (0.63%)	1 / 319 (0.31%)	3 / 314 (0.96%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	7 / 317 (2.21%)	6 / 319 (1.88%)	5 / 314 (1.59%)
occurrences causally related to treatment / all	0 / 7	0 / 6	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pyelonephritis			
subjects affected / exposed	2 / 317 (0.63%)	0 / 319 (0.00%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Sepsis			
subjects affected / exposed	5 / 317 (1.58%)	0 / 319 (0.00%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 317 (0.32%)	1 / 319 (0.31%)	5 / 314 (1.59%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
COVID-19			
subjects affected / exposed	6 / 317 (1.89%)	7 / 319 (2.19%)	4 / 314 (1.27%)
occurrences causally related to treatment / all	0 / 6	0 / 8	0 / 4
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 0
Gastroenteritis viral			

subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Localised infection			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lyme disease			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Nasopharyngitis			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Osteomyelitis chronic			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	0 / 314 (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
Pneumonia viral			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyoderma			

subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic endorgan damage			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 317 (0.00%)	1 / 319 (0.31%)	2 / 314 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	2 / 317 (0.63%)	3 / 319 (0.94%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			

subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 317 (0.32%)	0 / 319 (0.00%)	0 / 314 (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
Failure to thrive			
subjects affected / exposed	0 / 317 (0.00%)	0 / 319 (0.00%)	1 / 314 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	A: Faricimab 6 mg Q8W	B: Faricimab 6 mg PTI	C: Aflibercept 2 mg Q8W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	195 / 317 (61.51%)	169 / 319 (52.98%)	178 / 314 (56.69%)
Investigations			
Intraocular pressure increased			
subjects affected / exposed	21 / 317 (6.62%)	14 / 319 (4.39%)	15 / 314 (4.78%)
occurrences (all)	34	23	27
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	18 / 317 (5.68%)	8 / 319 (2.51%)	14 / 314 (4.46%)
occurrences (all)	23	8	19
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 317 (6.31%)	26 / 319 (8.15%)	16 / 314 (5.10%)
occurrences (all)	22	29	16
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 317 (5.68%)	11 / 319 (3.45%)	8 / 314 (2.55%)
occurrences (all)	36	16	10
Eye disorders			

Cataract			
subjects affected / exposed	52 / 317 (16.40%)	58 / 319 (18.18%)	33 / 314 (10.51%)
occurrences (all)	77	88	48
Conjunctival haemorrhage			
subjects affected / exposed	36 / 317 (11.36%)	24 / 319 (7.52%)	25 / 314 (7.96%)
occurrences (all)	44	29	34
Diabetic retinal oedema			
subjects affected / exposed	29 / 317 (9.15%)	25 / 319 (7.84%)	23 / 314 (7.32%)
occurrences (all)	31	30	27
Vitreous detachment			
subjects affected / exposed	19 / 317 (5.99%)	18 / 319 (5.64%)	27 / 314 (8.60%)
occurrences (all)	26	21	30
Dry eye			
subjects affected / exposed	19 / 317 (5.99%)	22 / 319 (6.90%)	11 / 314 (3.50%)
occurrences (all)	34	39	24
Vitreous floaters			
subjects affected / exposed	17 / 317 (5.36%)	12 / 319 (3.76%)	18 / 314 (5.73%)
occurrences (all)	22	15	21
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 317 (4.73%)	16 / 319 (5.02%)	10 / 314 (3.18%)
occurrences (all)	15	17	10
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	17 / 317 (5.36%)	7 / 319 (2.19%)	3 / 314 (0.96%)
occurrences (all)	17	7	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	30 / 317 (9.46%)	27 / 319 (8.46%)	38 / 314 (12.10%)
occurrences (all)	35	34	43
Urinary tract infection			
subjects affected / exposed	14 / 317 (4.42%)	15 / 319 (4.70%)	27 / 314 (8.60%)
occurrences (all)	20	18	35

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2018	- Protocol GR40398 has been amended to include additional prohibited medications (Section 4.4.2) and more detailed examples of contraceptive methods for females of childbearing potential (Section 4.1.1.1) to enhance patient safety and to comply with health authority requests, enabling this protocol to be conducted globally. - A China-specific addendum to Protocol GR40398, Version 2 to support the enrollment of patients from China (in both the global and China extension phases) removed the following optional sample collections from Chinese patients: aqueous humor sample, vitreous sample, PD plasma samples, samples for Research Biosample Repository, and DNA sample.
20 June 2019	- The number of patients and sites has been added for the China enrollment plan.; - The study eye ocular exclusion criterion has been modified to include vitreomacular traction, which will be evaluated by the CRC for eligibility.; - The concurrent ocular conditions exclusion criterion has been modified to include retinal embolus.; - A section for risks associated with aflibercept has been added.; - Study treatment interruption due to active or suspected infection has been expanded to include "suspected ocular or periocular infections".; - Criteria for study treatment interruption due to IOI have been updated such that study treatment may be resumed subsequently as determined by the investigator.; - Reporting of medication errors and associated adverse event in Section 5.4.4 was updated and moved to Section 5.3.5.12. The medication errors themselves will no longer be reported expeditiously (within 24 hours). However, if they cause a serious adverse event or adverse event of special interest, these will continue to be reported in an expedited manner.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

All secondary outcome measures were unpowered for statistical analysis, and the results should be interpreted with caution.

Notes: