Clinical trial results:
A Multicenter, Open-Label Extension Study to Evaluate the Long-Term Safety and Tolerability of Faricimab in Patients With Neovascular Age-Related Macular Degeneration (AVONELLE-X)

Summary

EudraCT number	2020-004523-16
Trial protocol	FR PT DE AT DK HU PL NL IT BG
Global end of trial date	03 September 2024

Results information

Result version number	v1
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	GR42691

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04777201
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche, Ltd.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4058
Public contact	F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2024
Global end of trial reached?	Yes
Global end of trial date	03 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the main study was to evaluate the long-term ocular and systemic safety and tolerability of faricimab in all patients who enrolled in the long-term extension study. The primary objective of the substudy was to evaluate the impact of faricimab on corneal endothelial cell health, as assessed by specular microscopy.

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 applicable laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 April 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 54
Country: Number of subjects enrolled	Australia: 21
Country: Number of subjects enrolled	Austria: 12
Country: Number of subjects enrolled	Bulgaria: 5
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Canada: 26
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Hong Kong: 9
Country: Number of subjects enrolled	Hungary: 42
Country: Number of subjects enrolled	Israel: 22
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Japan: 98
Country: Number of subjects enrolled	Korea, Republic of: 31
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Poland: 61
Country: Number of subjects enrolled	Portugal: 8

Country: Number of subjects enrolled	Russian Federation: 26
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Spain: 47
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	Türkiye: 18
Country: Number of subjects enrolled	United Kingdom: 37
Country: Number of subjects enrolled	United States: 434
Worldwide total number of subjects	1029
EEA total number of subjects	227

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)	78
From 65 to 84 years	746
85 years and over	205

Subject disposition

Recruitment

Recruitment details:

A total of 1036 participants were enrolled in the main study, 7 of whom were excluded from analysis as an outcome of the GCP non-compliance audit finding, resulting in a final analysis set of 1029 participants. A subgroup of 117 also participanted concurrently in the substudy.

Pre-assignment

Screening details:

A total of 7 patients were not included in the analysis set prior to assignment. This was a precautionary measure following a Good Clinical Practice (GCP) non-compliance audit finding at a single clinical trial site for a different investigational product.

Period 1

Period 1 title	Main Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Main Study Cohort A: Faricimab PTI (Prior Faricimab)

Arm description:

This cohort included participants previously randomized to Arm A (faricimab up to every 16 weeks [Q16W]) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

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

Dosage and administration details:

Faricimab 6 mg will be administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Arm title	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)

Arm description:

This cohort included participants previously randomized to Arm B (aflibercept 2 mg Q8W) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

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

Dosage and administration details:

Faricimab 6 mg will be administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Number of subjects in period 1	Main Study Cohort A: Faricimab PTI (Prior Faricimab)	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)
Started	524	505
Safety-Evaluable Population	520	505
Completed	453	415
Not completed	71	90
Adverse event, serious fatal	13	27
Consent withdrawn by subject	19	27
Physician decision	8	10
Adverse event, non-fatal	8	8
Subject missed the safety follow-up visit	9	10
Lost to follow-up	9	4
Reason not specified	3	3
Lack of efficacy	1	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Main Study Cohort A: Faricimab PTI (Prior Faricimab)

Reporting group description:

This cohort included participants previously randomized to Arm A (faricimab up to every 16 weeks [Q16W]) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Reporting group title	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)

Reporting group description:

This cohort included participants previously randomized to Arm B (aflibercept 2 mg Q8W) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Reporting group values	Main Study Cohort A: Faricimab PTI (Prior Faricimab)	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)	Total
Number of subjects	524	505	1029
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)	41	37	78
From 65-84 years	398	348	746
85 years and over	85	120	205
Age Continuous Units: Years			
arithmetic mean	76.4	77.7	
standard deviation	± 8.2	± 8.8	-
Sex: Female, Male Units: Participants			
Female	308	291	599
Male	216	214	430
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	50	53	103
Not Hispanic or Latino	463	445	908
Unknown or Not Reported	11	7	18
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	2	4
Asian	76	83	159
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	1	5	6
White	433	402	835
More than one race	0	1	1
Unknown or Not Reported	12	12	24

Subject analysis sets

Subject analysis set title	Substudy: Faricimab PTI in the Study Eye
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This analysis group represents the results for the substudy participants' study eyes. Participants from the main long-term extension study who also consented to participate in this substudy received faricimab 6 mg by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Subject analysis set title	Substudy: Fellow Eye
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This analysis group represents the results for the substudy participants' fellow (non-study) eyes. The fellow eyes of enrolled participants in the substudy were used as a comparator. At the discretion of the principal investigator, fellow eyes were allowed to be treated with standard of care anti-VEGF therapy (if needed) according to region-specific prescribing information. Administration of the following therapies to the fellow eye were prohibited during the substudy: faricimab, brolucizumab, bevacizumab, and Port Delivery System implantation.

Subject analysis set title	Substudy: Faricimab PTI
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants from the main long-term extension study who also consented to participate in this substudy received faricimab 6 mg by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study. The fellow eyes of enrolled participants in the substudy were used as a comparator. At the discretion of the principal investigator, fellow eyes were allowed to be treated with standard of care anti-VEGF therapy (if needed) according to region-specific prescribing information. Administration of the following therapies to the fellow eye were prohibited during the substudy: faricimab, brolucizumab, bevacizumab, and Port Delivery System implantation.

Reporting group values	Substudy: Faricimab PTI in the Study Eye	Substudy: Fellow Eye	Substudy: Faricimab PTI
Number of subjects	113	113	113
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			75.6
standard deviation	±	±	± 8.1

Sex: Female, Male Units: Participants			
Female			61
Male			52
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino			23
Not Hispanic or Latino			90
Unknown or Not Reported			0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native			0
Asian			0
Native Hawaiian or Other Pacific Islander			0
Black or African American			1
White			112
More than one race			0
Unknown or Not Reported			0

End points

End points reporting groups

Reporting group title	Main Study Cohort A: Faricimab PTI (Prior Faricimab)

Reporting group description:

This cohort included participants previously randomized to Arm A (faricimab up to every 16 weeks [Q16W]) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Reporting group title	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)

Reporting group description:

This cohort included participants previously randomized to Arm B (aflibercept 2 mg Q8W) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Subject analysis set title	Substudy: Faricimab PTI in the Study Eye
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This analysis group represents the results for the substudy participants' study eyes. Participants from the main long-term extension study who also consented to participate in this substudy received faricimab 6 mg by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Subject analysis set title	Substudy: Fellow Eye
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

This analysis group represents the results for the substudy participants' fellow (non-study) eyes. The fellow eyes of enrolled participants in the substudy were used as a comparator. At the discretion of the principal investigator, fellow eyes were allowed to be treated with standard of care anti-VEGF therapy (if needed) according to region-specific prescribing information. Administration of the following therapies to the fellow eye were prohibited during the substudy: faricimab, brolucizumab, bevacizumab, and Port Delivery System implantation.

Subject analysis set title	Substudy: Faricimab PTI
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants from the main long-term extension study who also consented to participate in this substudy received faricimab 6 mg by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study. The fellow eyes of enrolled participants in the substudy were used as a comparator. At the discretion of the principal investigator, fellow eyes were allowed to be treated with standard of care anti-VEGF therapy (if needed) according to region-specific prescribing information. Administration of the following therapies to the fellow eye were prohibited during the substudy: faricimab, brolucizumab, bevacizumab, and Port Delivery System implantation.

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

End point title	Incidence and Severity of Ocular Adverse Events in the Study Eye, with Severity Determined According to Adverse Event Severity Grading Scale[1]

End point description:

This is an analysis of participants with at least one ocular adverse event (AE) that occurred in the study eye. Investigators sought information on AEs at each contact with the participants. All AEs were recorded and the investigator made an assessment of the seriousness, severity (e.g., mild, moderate, or severe intensity), and causality for each AE. AEs of special interest (AESI) included the following: Sight-threatening AEs that cause a drop in visual acuity (VA) score ≥30 letters lasting more than 1 hour, are associated with severe intraocular inflammation (IOI), or require surgical or medical intervention to prevent permanent loss of sight; suspected transmission of an infectious agent by the study drug; and, 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	Primary

End point timeframe:

From the date of first administration of faricimab through 28 days after the end of study (up to 2 years)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned. The adverse events were summarized descriptively.

End point values	Main Study Cohort A: Faricimab PTI (Prior Faricimab)	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)	Substudy: Faricimab PTI	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	520	505	113	
Units: participants				
Any Adverse Event (AE), Any Severity	188	207	16	
AEs by Severity: Mild	114	106	11	
AEs by Severity: Moderate	58	75	4	
AEs by Severity: Severe	13	23	1	
AEs by Severity: Missing	3	3	0	
Serious Adverse Event (SAE)	18	27	1	
AE Leading to Withdrawal from Study Treatment	4	5	0	
Treatment-related AE	8	12	2	
Treatment-related SAE	1	3	1	
Any AE of Special Interest (AESI)	15	21	1	
AESI: Drop in Visual Acuity Score ≥30 Letters	11	16	1	
AESI: Associated with Severe IOI	1	2	0	
AESI: Intervention Req. to Prev. Perm. Vision Loss	3	3	0	
AESI: Suspect. Transm. of Infectious Agent by Drug	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Ocular Adverse Events in the Fellow Eye

End point title	Incidence of Ocular Adverse Events in the Fellow Eye[2]

End point description:

This is an analysis of participants with at least one ocular adverse event (AE) that occurred in the study eye. Investigators sought information on AEs at each contact with the participants. All AEs were recorded and the investigator made an assessment of the seriousness, severity, and causality for each AE. AEs of special interest (AESI) included the following: Sight-threatening AEs that cause a drop in visual acuity (VA) score ≥30 letters lasting more than 1 hour, are associated with severe intraocular inflammation (IOI), or require surgical or medical intervention to prevent permanent loss of sight; suspected transmission of an infectious agent by the study drug; and, 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	Primary

End point timeframe:

From the date of first administration of faricimab through 28 days after the end of study (up to 2 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned. The adverse events were summarized descriptively.

End point values	Main Study Cohort A: Faricimab PTI (Prior Faricimab)	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)	Substudy: Faricimab PTI	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	520	505	113	
Units: participants				
Any Adverse Event (AE), Any Severity	157	149	17	
Serious Adverse Event (SAE)	4	11	1	
Any AE of Special Interest (AESI)	3	11	1	
AESI: Drop in Visual Acuity Score ≥30 Letters	3	8	0	
AESI: Associated with Severe IOI	0	0	0	
AESI: Intervention Req. to Prev. Perm. Vision Loss	0	3	1	
AESI: Suspect. Transm. of Infectious Agent by Drug	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Incidence and Severity of Non-Ocular Adverse Events, with Severity Determined According to Adverse Event Severity Grading Scale

End point title	Incidence and Severity of Non-Ocular Adverse Events, with Severity Determined According to Adverse Event Severity Grading Scale[3]

End point description:

This is an analysis of participants with at least one non-ocular (systemic) adverse event (AE). Investigators sought information on AEs at each contact with the participants. All AEs were recorded and the investigator made an assessment of the seriousness, severity (e.g., mild, moderate, or severe intensity), and causality for each AE. AEs of special interest (AESI) included the following: Sight-threatening AEs that cause a drop in visual acuity (VA) score ≥30 letters lasting more than 1 hour, are associated with severe intraocular inflammation (IOI), or require surgical or medical intervention to prevent permanent loss of sight; suspected transmission of an infectious agent by the study drug; and, 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	Primary

End point timeframe:

From the date of first administration of faricimab through 28 days after the end of study (up to 2 years)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned. The adverse events were summarized descriptively.

End point values	Main Study Cohort A: Faricimab PTI (Prior Faricimab)	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)	Substudy: Faricimab PTI	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	520	505	113	
Units: participants				
Any Adverse Event (AE), Any Severity	343	337	41	
AE by Severity: Mild	122	120	15	
AE by Severity: Moderate	138	124	17	
AE by Severity: Severe	83	93	9	
Serious Adverse Event (SAE)	110	127	13	
AE Leading to Withdrawal from Study Treatment	3	9	0	
Any AE of Special Interest (AESI)	0	0	0	
AESI: High ALT/AST & High Bilir. or Clin. Jaundice	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Substudy: Percent Change in Corneal Endothelial Cell Density From Baseline at 1 Year in the Study Eye as Compared With the Fellow Eye

End point title	Substudy: Percent Change in Corneal Endothelial Cell Density From Baseline at 1 Year in the Study Eye as Compared With the Fellow Eye

End point description:

Specular microscopy was performed for both eyes prior to application of any topical ophthalmic anesthetic, tonometry, or any other study treatment on the same day for the evaluation of corneal endothelial cell density. The 1-year timepoint was defined as the earliest substudy visit closest to Week 52 occurring between Week 48 and Week 64. Data (from both study eye and fellow eye) collected after the fellow eye's use of prohibited therapies—such as faricimab, brolucizumab, bevacizumab, and Port Delivery System implantation—were excluded from the corneal endothelial cell analysis. Modified Intent-to-Treat Population: All enrolled participants who received at least one injection of faricimab in the study eye during this substudy. Only participants who completed the Year 1 visit within the analysis window (Weeks 48 to 64) were included for analysis.

End point type	Primary

End point timeframe:

Baseline and 1 year

End point values	Substudy: Faricimab PTI in the Study Eye	Substudy: Fellow Eye		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99	99		
Units: Percent change in cell density				
number (confidence interval 95%)	-0.51 (-1.68 to 0.65)	-0.71 (-1.53 to 0.10)		

Statistical analyses

Statistical analysis title	Difference in Percent Change CEC Denisty at 1 Year

Statistical analysis description:

No formal hypothesis testing was planned for this study. The paired t-tests were for reference purposes and thus not considered formal. The test was 2-sided, with the null hypothesis of no difference in percent change from baseline between the study eye and fellow eye in each patient.

Comparison groups	Substudy: Faricimab PTI in the Study Eye v Substudy: Fellow Eye
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7702
Method	Paired t-test
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	1.54

Secondary: Substudy: Percent Change in Corneal Endothelial Cell Density From Baseline at Week 24 in the Study Eye as Compared With the Fellow Eye

End point title	Substudy: Percent Change in Corneal Endothelial Cell Density From Baseline at Week 24 in the Study Eye as Compared With the Fellow Eye

End point description:

Specular microscopy was performed for both eyes prior to application of any topical ophthalmic anesthetic, tonometry, or any other study treatment on the same day for the evaluation of corneal endothelial cell density. The Week 24 timepoint was defined as the earliest substudy visit closest to Week 24 occurring between Week 20 and Week 28. Data (from both study eye and fellow eye) collected after the fellow eye's use of prohibited therapies—such as faricimab, brolucizumab, bevacizumab, and Port Delivery System implantation—were excluded from the corneal endothelial cell analysis. Modified Intent-to-Treat Population: All enrolled participants who received at least one injection of faricimab in the study eye during this substudy. Only participants who completed the midpoint visit within the analysis window (Weeks 20 to 28) were included for analysis.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Substudy: Faricimab PTI in the Study Eye	Substudy: Fellow Eye		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	103	103		
Units: Percent change in cell density				
number (confidence interval 95%)	-0.02 (-0.86 to 0.81)	-0.29 (-0.92 to 0.81)		

Statistical analyses

Statistical analysis title	Difference in Percent Change CEC Density, 24 Weeks
Statistical analysis description:	
No formal hypothesis testing was planned for this study. The paired t-tests were for reference purposes and thus not considered formal. The test was 2-sided, with the null hypothesis of no difference in percent change from baseline between the study eye and fellow eye in each patient.	
Comparison groups	Substudy: Faricimab PTI in the Study Eye v Substudy: Fellow Eye
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6305
Method	Paired t-test
Parameter estimate	Mean difference (final values)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	1.38

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first administration of faricimab through 28 days after the end of study (up to 2 years)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Main Study Cohort A: Faricimab PTI (Prior Faricimab)

Reporting group description:

This cohort included participants previously randomized to Arm A (faricimab up to every 16 weeks [Q16W]) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Reporting group title	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)

Reporting group description:

This cohort included participants previously randomized to Arm B (aflibercept Q8W) in the parent studies [GR40306 (NCT03823287) or GR40844 (NCT03823300)]. In this long-term extension study, faricimab 6 mg was administered by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study.

Reporting group title	Substudy: Faricimab PTI

Reporting group description:

Participants from the main long-term extension study who also consented to participate in this substudy received faricimab 6 mg by intravitreal (IVT) injection into the study eye according to the personalized treatment interval (PTI) dosing regimen for the duration of the study. The fellow eyes of enrolled participants in the substudy were used as a comparator. At the discretion of the principal investigator, fellow eyes were allowed to be treated with standard of care anti-VEGF therapy (if needed) according to region-specific prescribing information. Administration of the following therapies to the fellow eye were prohibited during the substudy: faricimab, brolucizumab, bevacizumab, and Port Delivery System implantation.

Serious adverse events	Main Study Cohort A: Faricimab PTI (Prior Faricimab)	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)	Substudy: Faricimab PTI
Total subjects affected by serious adverse events			
subjects affected / exposed	125 / 520 (24.04%)	156 / 505 (30.89%)	14 / 113 (12.39%)
number of deaths (all causes)	13	27	1
number of deaths resulting from adverse events	13	27	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ameloblastoma			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Basal cell carcinoma			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Bladder neoplasm			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Brain cancer metastatic			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Brain neoplasm			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Breast cancer			
subjects affected / exposed	4 / 520 (0.77%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Cholangiocarcinoma			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Colon cancer			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Colon neoplasm			

subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Colorectal adenocarcinoma			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Cervix carcinoma			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Gastric cancer			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Eyelid tumour			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Gastric neoplasm			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Lung neoplasm			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Lung carcinoma cell type unspecified stage IV			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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 cancer metastatic			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Lung adenocarcinoma			
subjects affected / exposed	2 / 520 (0.38%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Mantle cell lymphoma			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Pancreatic carcinoma			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Metastatic neoplasm			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Metastases to lung			

subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Meningioma benign			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Meningioma			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	2 / 520 (0.38%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic adenoma			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Prostate cancer recurrent			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Small cell carcinoma			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral cancer recurrent			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Transitional cell carcinoma			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Tongue neoplasm malignant stage unspecified			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Small cell lung cancer			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Intermittent claudication			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Aortic stenosis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Giant cell arteritis			

subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Hypotension			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Peripheral artery thrombosis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Peripheral artery occlusion			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Peripheral ischaemia			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Surgical and medical procedures			
Knee arthroplasty			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Death			
subjects affected / exposed	1 / 520 (0.19%)	3 / 505 (0.59%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Physical deconditioning			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Acquired hydrocele			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Prostatic disorder			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 520 (0.19%)	4 / 505 (0.79%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Bronchial hyperreactivity			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chronic respiratory failure			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Dyspnoea			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Pleural effusion			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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

Pulmonary oedema			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 520 (0.58%)	0 / 505 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Depressive delusion			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Confusional state			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Delirium			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Device loosening			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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 sodium decreased			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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 murmur			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Inflammatory marker increased			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Influenza A virus test positive			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Injury, poisoning and procedural complications			
Failed back surgery syndrome			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Contusion			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Concussion			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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

Compression fracture			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Fall			
subjects affected / exposed	4 / 520 (0.77%)	7 / 505 (1.39%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Femoral neck fracture			
subjects affected / exposed	2 / 520 (0.38%)	2 / 505 (0.40%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Hip fracture			
subjects affected / exposed	3 / 520 (0.58%)	3 / 505 (0.59%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Rib fracture			

subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Postoperative wound complication			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Pneumothorax traumatic			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Periprosthetic fracture			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Pelvic fracture			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Meniscus injury			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Humerus fracture			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Injury			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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 limb fracture			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Subdural haematoma			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Stoma obstruction			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Skeletal injury			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Shoulder fracture			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Toxicity to various agents			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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 disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Acute myocardial infarction			

subjects affected / exposed	1 / 520 (0.19%)	4 / 505 (0.79%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve stenosis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Atrial fibrillation			
subjects affected / exposed	3 / 520 (0.58%)	5 / 505 (0.99%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Cardiac failure congestive			
subjects affected / exposed	6 / 520 (1.15%)	7 / 505 (1.39%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 6	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	3 / 520 (0.58%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Myocardial infarction			
subjects affected / exposed	2 / 520 (0.38%)	6 / 505 (1.19%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 4	0 / 0
Coronary artery stenosis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Coronary artery disease			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Chronic left ventricular failure			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Cardiovascular disorder			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Sinus node dysfunction			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Nervous system disorders			
Carotid artery stenosis			

subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Balance disorder			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Aphasia			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Cerebral infarction			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Cerebrovascular accident			
subjects affected / exposed	5 / 520 (0.96%)	5 / 505 (0.99%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	1 / 5	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Drop attacks			

subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Dizziness			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Dementia Alzheimer's type			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Cognitive disorder			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Encephalopathy			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular dementia			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Nerve compression			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Myasthenia gravis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Hypoaesthesia			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Blood and lymphatic system disorders			
Anaemia vitamin B12 deficiency			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Anaemia			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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			
Dry age-related macular degeneration			
subjects affected / exposed	3 / 520 (0.58%)	0 / 505 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Choroidal neovascularisation			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Choroidal detachment			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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			
subjects affected / exposed	5 / 520 (0.96%)	7 / 505 (1.39%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 5	2 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Age-related macular degeneration			
subjects affected / exposed	2 / 520 (0.38%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dry eye			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-infectious endophthalmitis			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neovascular age-related macular degeneration			
subjects affected / exposed	4 / 520 (0.77%)	14 / 505 (2.77%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 14	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iridocyclitis			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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 aneurysm			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Subretinal fibrosis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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 tear			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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 pigment epithelial tear			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal degeneration			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Visual acuity reduced			
subjects affected / exposed	3 / 520 (0.58%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uveitis			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic gastritis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Colitis			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Colitis ulcerative			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Diverticulum intestinal			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Gastric ulcer			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Duodenogastric reflux			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Duodenitis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Intestinal dilatation			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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 haemorrhage			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Gastritis			

subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Intestinal ischaemia			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Intestinal obstruction			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Small intestinal obstruction			
subjects affected / exposed	2 / 520 (0.38%)	0 / 505 (0.00%)	0 / 113 (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
Pancreatitis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Irritable bowel syndrome			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Large intestine polyp			
subjects affected / exposed	1 / 520 (0.19%)	2 / 505 (0.40%)	0 / 113 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			

subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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 and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 520 (0.58%)	4 / 505 (0.79%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder perforation			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Haematuria			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Nephritic syndrome			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Nephrolithiasis			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Renal colic			

subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Renal failure			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Urinary retention			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Musculoskeletal and connective tissue disorders			
Haematoma muscle			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Musculoskeletal disorder			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Rhabdomyolysis			

subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Rheumatoid arthritis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Spondylolisthesis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Synovial cyst			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Osteoarthritis			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 520 (0.19%)	1 / 505 (0.20%)	0 / 113 (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
Arthritis bacterial			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Bronchitis bacterial			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Bronchitis			

subjects affected / exposed	2 / 520 (0.38%)	1 / 505 (0.20%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	8 / 520 (1.54%)	5 / 505 (0.99%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 520 (0.19%)	3 / 505 (0.59%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Pseudomonal bacteraemia			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 520 (0.38%)	3 / 505 (0.59%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Febrile infection			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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			

subjects affected / exposed	6 / 520 (1.15%)	9 / 505 (1.78%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Dermo-hypodermitis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Endophthalmitis			
subjects affected / exposed	2 / 520 (0.38%)	3 / 505 (0.59%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Viral uveitis			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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	3 / 520 (0.58%)	4 / 505 (0.79%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Septic shock			

subjects affected / exposed	3 / 520 (0.58%)	2 / 505 (0.40%)	0 / 113 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 520 (0.00%)	0 / 505 (0.00%)	1 / 113 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Electrolyte imbalance			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Hyponatraemia			
subjects affected / exposed	0 / 520 (0.00%)	2 / 505 (0.40%)	0 / 113 (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
Hypophosphataemia			
subjects affected / exposed	0 / 520 (0.00%)	1 / 505 (0.20%)	0 / 113 (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
Malnutrition			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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
Starvation			
subjects affected / exposed	1 / 520 (0.19%)	0 / 505 (0.00%)	0 / 113 (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

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

Non-serious adverse events	Main Study Cohort A: Faricimab PTI (Prior Faricimab)	Main Study Cohort B: Faricimab PTI (Prior Aflibercept)	Substudy: Faricimab PTI
Total subjects affected by non-serious adverse events			
subjects affected / exposed	158 / 520 (30.38%)	169 / 505 (33.47%)	9 / 113 (7.96%)
Eye disorders			
Cataract			
subjects affected / exposed	56 / 520 (10.77%)	63 / 505 (12.48%)	2 / 113 (1.77%)
occurrences (all)	78	80	2
Posterior capsule opacification			
subjects affected / exposed	14 / 520 (2.69%)	26 / 505 (5.15%)	1 / 113 (0.88%)
occurrences (all)	17	30	1
Neovascular age-related macular degeneration			
subjects affected / exposed	60 / 520 (11.54%)	55 / 505 (10.89%)	2 / 113 (1.77%)
occurrences (all)	70	65	3
Infections and infestations			
COVID-19			
subjects affected / exposed	61 / 520 (11.73%)	48 / 505 (9.50%)	5 / 113 (4.42%)
occurrences (all)	65	49	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2021	Version 2: -The EUDRACT number, 2020-004523-16, and the study name, AVONELLE-X, have been added to the protocol cover page, protocol acceptance form, and protocol synopsis.; -Section 4.5.6.1 and Appendix 1 have been updated to specify that the optional aqueous humor is to be collected from the study eye.; -A Safety Follow-up visit has been added after the final dose of study treatment to ensure adequate patient safety monitoring.; -Appendix 1 has been updated to remove the optional pharmacokinetic (PK) plasma sample collection at Week 12 as this sample was a duplicate to the mandatory plasma PK sample collected at the same visit.
15 July 2022	Version 3: -The option of a dosing interval of Q4W was added to the PTI algorithm.; -Instructions were added that it is not possible for a site to manually modify the PTI algorithm to adjust the faricimab treatment interval.; -The definition for baseline was revised to Day 1 of this study for patients randomized to faricimab in the parent study and as the first day of faricimab treatment for patients randomized to aflibercept in the parent study.; -The risks associated with faricimab were updated to align with Faricimab IB version 11.; -The timeframe for the exclusion of patients who were pregnant or breastfeeding, or intending to become pregnant was extended from within 28 days to within 3 months after the final dose.; -The window for early termination visit was updated to a minimum of 28 days after receiving the final dose of study drug.; -The timing of reporting AEs, SAEs, and AESIs was revised to begin after enrollment in this study, not after initiation of study drug.; -The reporting of AEs associated with a special situation that also qualify as AESI has been revised and should be reported to the Sponsor within 24 hours.; -To align with the responsibility of the PI for the overall safety of the patients, it was clarified that the treatment administrator must be an ophthalmologist, and, ideally, a retina specialist, and it is the PI's responsibility to ensure that the treatment administrator is suitably qualified.; -Therapies that claim to have an effect on macular pathology (e.g., kallidinogenase) were added as a prohibited therapy.; -The types of ocular assessments were clarified, with ultra-wide photography of CFP and FFA imaging permitted only when no other alternative is available.; -The purpose of unscheduled safety visits was revised, specifying that they should only be used for the assessment of AEs and are not intended for standard-of-care procedures.; -CFP was added as an assessment that may be performed during an unscheduled safety assessment visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported