Clinical trial results:
A Randomized, Double-masked, Phase 3 Study of ABP 938 Efficacy and Safety Compared to Aflibercept (Eylea(R)) in Subjects with Neovascular Age-related Macular Degeneration

Summary

EudraCT number	2019-002503-17
Trial protocol	DE LV EE SK ES CZ LT PL IT
Global end of trial date	30 January 2023

Results information

Result version number	v1 (current)
This version publication date	29 December 2023
First version publication date	29 December 2023

Trial information

Trial identification

Sponsor protocol code	20170542

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04270747
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	Study Director, Amgen Inc., +1 8665726436, medinfo@amgen.com
Scientific contact	Study Director, Amgen Inc., +1 8665726436, medinfo@amgen.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	30 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess the efficacy of ABP 938 compared to aflibercept.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation Good Clinical Practice regulations/guidelines.

Background therapy: -

Evidence for comparator:

Eylea (aflibercept) belongs to the pharmacologic class of vascular endothelial growth factor (VEGF) inhibitors. In the United States and the European Union, Eylea (aflibercept) is approved for intravitreal (IVT) administration in the treatment of neovascular (wet) age-related macular degeneration.

Actual start date of recruitment	22 June 2020
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	Korea, Republic of: 37
Country: Number of subjects enrolled	Japan: 25
Country: Number of subjects enrolled	Hong Kong: 12
Country: Number of subjects enrolled	Hungary: 90
Country: Number of subjects enrolled	Poland: 55
Country: Number of subjects enrolled	Germany: 30
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	Czechia: 24
Country: Number of subjects enrolled	Israel: 18
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	Estonia: 12
Country: Number of subjects enrolled	Latvia: 11
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	United States: 194
Country: Number of subjects enrolled	Canada: 5
Worldwide total number of subjects	576
EEA total number of subjects	285

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)	49
From 65 to 84 years	449
85 years and over	78

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 102 centers in Canada, Czech Republic, Estonia, Germany, Hong Kong, Hungary, Israel, Italy, Japan, South Korea, Latvia, Lithuania, Poland, Slovakia, Spain, and the United States between 22 June 2020 and 30 January 2023.

Pre-assignment

Screening details:

Both eyes were assessed at the screening visit for eligibility, and only 1 eye was selected from each participant as the study eye. If both eyes met the eligibility criteria, the study eye was the one with the worse best corrected visual acuity (BCVA).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	ABP 938

Arm description:

Participants were randomized to receive 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and remained on ABP 938 dosing every 8 weeks from Week 16 until Week 48.

Arm type	Experimental
Investigational medicinal product name	ABP 938
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravitreal use

Dosage and administration details:

Administered by IVT injection.

Arm title	Aflibercept

Arm description:

Participants were randomized to receive 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and were re-randomized to receive aflibercept or ABP 938 dosing every 8 weeks from Week 16 until Week 48.

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:

Administered by IVT injection.

Number of subjects in period 1	ABP 938	Aflibercept
Started	288	288
Completed Through Week 16	273	270
Received ABP 938 Post Week 16	273	133 [1]
Received Aflibercept Post Week 16	0 [2]	136 [3]
Completed	251	248
Not completed	37	40
Adverse event, serious fatal	2	4
Physician decision	4	3
Adverse event, non-fatal	8	8
Miscellaneous	2	2
Protocol Specified Criteria	6	7
Requirement for Alternative Dosing Schedule	2	1
Lost to follow-up	4	1
Requirement for Alternative Therapy	1	-
Consent Withdrawn	7	12
Protocol deviation	1	2

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants included in ABP 938 or aflibercept milestone post Week 16.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Milestone N/A for ABP 938 arm.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Participants included in ABP 938 or aflibercept milestone post Week 16.

Baseline characteristics

Reporting groups	
Reporting group title	ABP 938
Reporting group description:	
Participants were randomized to receive 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and remained on ABP 938 dosing every 8 weeks from Week 16 until Week 48.	
Reporting group title	Aflibercept
Reporting group description:	
Participants were randomized to receive 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and were re-randomized to receive aflibercept or ABP 938 dosing every 8 weeks from Week 16 until Week 48.	

Reporting group values	ABP 938	Aflibercept	Total
Number of subjects	288	288	576
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	76.0	76.0	
standard deviation	± 7.93	± 7.95	-
Sex: Female, Male Units:			
Female	151	171	322
Male	137	117	254
Race/Ethnicity, Customized Units: Subjects			
Asian	36	39	75
Black or African American	1	1	2
Multiple	1	0	1
White	250	248	498
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	13	19
Not Hispanic or Latino	281	275	556
Unknown or Not Reported	1	0	1

End points

End points reporting groups

Reporting group title	ABP 938
Reporting group description:	
Participants were randomized to receive 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and remained on ABP 938 dosing every 8 weeks from Week 16 until Week 48.	
Reporting group title	Aflibercept
Reporting group description:	
Participants were randomized to receive 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and were re-randomized to receive aflibercept or ABP 938 dosing every 8 weeks from Week 16 until Week 48.	
Subject analysis set title	ABP 938 / ABP 938
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who were initially randomized to receive 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and remained on ABP 938 dosing every 8 weeks from Week 16 until Week 48.	
Subject analysis set title	Aflibercept / ABP 938
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who were initially randomized to receive 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) were re-randomized to receive 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 8 weeks from Week 16 until Week 48.	
Subject analysis set title	Aflibercept / Aflibercept
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who were initially randomized to receive 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8) and were re-randomized to receive aflibercept dosing every 8 weeks from Week 16 until Week 48.	
Subject analysis set title	Through Week 16: ABP 938
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants were treated with 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8).	
Subject analysis set title	Through Week 16: Aflibercept
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants were treated with 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8).	
Subject analysis set title	Post Week 16: ABP 938 / ABP 938
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who were initially treated with ABP 938 and remained on treatment with 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 8 weeks from Week 16 until Week 48.	
Subject analysis set title	Post Week 16: Aflibercept / ABP 938
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who were initially treated with aflibercept and were re-randomized and treated with 2 mg (0.05 mL) of ABP-938 by IVT injection in the study eye every 8 weeks from Week 16 until Week 48.	
Subject analysis set title	Post Week 16: Aflibercept / Aflibercept
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who were initially treated with aflibercept and were re-randomized and treated with 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 8 weeks from Week 16 until Week 48.

Primary: Mean Change from Baseline in BCVA at Week 8

End point title	Mean Change from Baseline in BCVA at Week 8

End point description:

BCVA score was assessed based on the number of letters read correctly on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart by the study eye at 4 meters. ETDRS letters score could range from 0 to 100 letters at each assessment.

A positive change from Baseline in ETDRS letter score indicated an improvement in visual acuity in the study eye. Change from Baseline calculated as observed post-baseline value - Baseline value.

Full Analysis Set: Consisted of all randomized participants, with treatment as the randomized treatment regardless of actual treatment received. Participants were included in the treatment group in which they were initially randomized. Analysis included participants with available data at Baseline and Week 8.

End point type	Primary

End point timeframe:

Baseline and Week 8

End point values	ABP 938	Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	281		
Units: Letters				
arithmetic mean (standard deviation)	6.4 (± 8.18)	6.5 (± 8.97)		

Statistical analyses

Statistical analysis title	ABP 938 versus (vs.) Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 8.

Estimated using analysis of covariance (ANCOVA) model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 v Aflibercept
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.1
upper limit	1.3

Secondary: Percentage of Participants who Maintained Vision at Week 52

End point title	Percentage of Participants who Maintained Vision at Week 52

End point description:

A participant was classified as maintaining vision if he/she lost fewer than 15 letters in ETDRS letter score, assessed in the study eye, compared to Baseline.

Full Analysis Set (Re-randomized): Consisted of all re-randomized participants, with treatment as the randomized treatment regardless of actual treatment received. Participants were included in the treatment group in which they were re-randomized. Analysis included participants with available data at Baseline and Week 52.

End point type	Secondary

End point timeframe:

Week 52

End point values	ABP 938 / ABP 938	Aflibercept / ABP 938	Aflibercept / Aflibercept	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	251	123	125	
Units: Percentage of Participants				
number (confidence interval 95%)	95.6 (93.1 to 98.2)	95.9 (92.5 to 99.4)	97.6 (94.9 to 100.0)	

Statistical analyses

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Risk difference in percentage of participants who maintained vision at Week 52.

Estimated using the stratified Newcombe confidence limits (with Mantel-Haenszel weights) adjusting for stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters).

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Risk difference (RD)
Point estimate	-2.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.2
upper limit	2.2

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Risk difference in percentage of participants who maintained vision at Week 52.

Estimated using the stratified Newcombe confidence limits (with Mantel-Haenszel weights) adjusting for stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters).

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Risk difference (RD)
Point estimate	-1.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.2
upper limit	2.8

Secondary: Mean Change from Baseline in BCVA

End point title	Mean Change from Baseline in BCVA

End point description:

BCVA score was assessed based on the number of letters read correctly on the ETDRS chart by the study eye at 4 meters. ETDRS letters score could range from 0 to 100 letters at each assessment.

A positive change from Baseline in ETDRS letter score indicated an improvement in visual acuity in the study eye. Change from Baseline calculated as observed post-baseline value - Baseline value.

Full Analysis Set (Re-randomized): Consisted of all randomized participants, with treatment as the re-randomized treatment regardless of actual treatment received. Participants were included in the treatment group in which they were re-randomized. Analysis included participants with available data at Baseline and at each timepoint.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 8, 16, 24, 32, 40, 48, and 52

End point values	ABP 938 / ABP 938	Aflibercept / ABP 938	Aflibercept / Aflibercept	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	273	134	136	
Units: Letters				
arithmetic mean (standard deviation)				
Week 4 (n = 272, 136, 131)	5.0 (± 6.57)	3.8 (± 8.19)	5.4 (± 8.35)	
Week 8 (n = 270, 134, 133)	6.5 (± 8.10)	5.6 (± 8.86)	7.6 (± 9.30)	
Week 16 (n = 273, 136, 134)	6.8 (± 8.69)	7.1 (± 9.32)	7.5 (± 9.31)	
Week 24 (n = 267, 136, 130)	7.2 (± 9.63)	7.0 (± 10.12)	7.1 (± 9.30)	
Week 32 (n = 263, 132, 131)	7.1 (± 11.00)	6.6 (± 11.11)	8.7 (± 9.21)	
Week 40 (n = 258, 130, 125)	7.3 (± 11.00)	7.9 (± 10.08)	8.1 (± 11.00)	
Week 48 (n = 251, 126, 123)	7.2 (± 11.51)	8.1 (± 10.74)	8.7 (± 10.84)	
Week 52 (n = 251, 125, 123)	7.6 (± 11.60)	8.0 (± 11.14)	9.4 (± 10.18)	

Statistical analyses

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 4.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.3
upper limit	1.2

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 8.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.3
upper limit	0.7

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 16.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.9
upper limit	1.2

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 24.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.3
upper limit	2.1

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 32.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.1
upper limit	0.5

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 40.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.3
upper limit	1.4

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 48.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.2
upper limit	0.8

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 52.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.5
Confidence interval	
level	Other: 2 %
sides	2-sided
lower limit	-3.4
upper limit	0.5

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 32.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4
upper limit	0.2

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 24.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.9
upper limit	2

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 4.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3
upper limit	0

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 8.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.6
upper limit	-0.2

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 16.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.1
upper limit	1.5

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 40.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.2
upper limit	2.2

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 48.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.9
upper limit	1.7

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 52.

Estimated using ANCOVA model adjusted for the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-3.5
upper limit	1.1

Secondary: Percentage of Participants who Gained at Least 10 Letters of Vision at Week 8

End point title	Percentage of Participants who Gained at Least 10 Letters of Vision at Week 8

End point description:

Percentage of participants who gained at least 10 letters of vision was assessed based on the number of letters read correctly on the ETDRS chart by the study eye at 4 meters. ETDRS letters score could range from 0 to 100 letters at each assessment.

Full Analysis Set: Consisted of all randomized participants, with treatment as the randomized treatment regardless of actual treatment received. Participants were included in the treatment group in which they were initially randomized. Analysis included participants with available data at Baseline and Week 8.

End point type	Secondary

End point timeframe:

Week 8

End point values	ABP 938	Aflibercept		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	281		
Units: Percentage of participants				
number (confidence interval 95%)	29.4 (24.1 to 34.7)	32.7 (27.3 to 38.2)		

Statistical analyses

Statistical analysis title	ABP 938 vs. Aflibercept

Statistical analysis description:

Risk difference in percentage of participants who gained at least 10 letters of vision at Week 8.

Estimated using the stratified Newcombe confidence limits (with Mantel-Haenszel weights) adjusting for stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters).

Comparison groups	ABP 938 v Aflibercept
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Risk difference (RD)
Point estimate	-3.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-9.8
upper limit	3.1

Secondary: Percentage of Participants who Gained at Least 15 Letters of Vision at Week 52

End point title	Percentage of Participants who Gained at Least 15 Letters of Vision at Week 52

End point description:

Percentage of participants who gained at least 15 letters of vision was assessed based on the number of letters read correctly on the ETDRS chart by the study eye at 4 meters. ETDRS letters score could range from 0 to 100 letters at each assessment.

Full Analysis Set (Re-randomized): Consisted of all re-randomized participants, with treatment as the randomized treatment regardless of actual treatment received. Participants were included in the treatment group in which they were re-randomized. Analysis included participants with available data at Baseline and Week 52.

End point type	Secondary

End point timeframe:

Week 52

End point values	ABP 938 / ABP 938	Aflibercept / ABP 938	Aflibercept / Aflibercept	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	251	123	125	
Units: Percentage of participants				
number (confidence interval 95%)	24.3 (19.0 to 29.6)	24.4 (16.8 to 32.0)	29.6 (21.6 to 37.6)	

Statistical analyses

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Risk difference in percentage of participants who gained at least 15 letters of vision at Week 52.

Estimated using the stratified Newcombe confidence limits (with Mantel-Haenszel weights) adjusting for stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters).

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Risk difference (RD)
Point estimate	-5.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.4
upper limit	4.2

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Risk difference in percentage of participants who gained at least 15 letters of vision at Week 52.

Estimated using the stratified Newcombe confidence limits (with Mantel-Haenszel weights) adjusting for stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters).

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Risk difference (RD)
Point estimate	-5.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-13.6
upper limit	2.5

Secondary: Mean Change from Baseline in Choroidal Neovascularization (CNV) Area Size

End point title	Mean Change from Baseline in Choroidal Neovascularization (CNV) Area Size

End point description:

CNV area size was measured by fluorescein angiography.

Change from Baseline calculated as observed post-baseline value - Baseline value.

Full Analysis Set (Re-randomized): Consisted of all randomized participants, with treatment as the re-randomized treatment regardless of actual treatment received. Participants were included in the treatment group in which they were re-randomized. Analysis included participants with available data at Baseline and at each timepoint.

End point type	Secondary

End point timeframe:

Baseline and Weeks 8, 16, 24, and 52

End point values	ABP 938 / ABP 938	Aflibercept / ABP 938	Aflibercept / Aflibercept	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	255	130	127	
Units: mm^2				
arithmetic mean (standard deviation)				
Week 8 (n = 255, 127, 130)	-4.962 (± 5.1604)	-5.169 (± 4.6943)	-5.479 (± 5.1023)	
Week 16 (n = 245, 121, 125)	-4.089 (± 5.3668)	-4.751 (± 4.8814)	-5.174 (± 5.2280)	
Week 24 (n = 242, 119, 118)	-4.323 (± 5.5972)	-5.121 (± 5.2776)	-5.308 (± 5.6238)	
Week 52 (n = 234, 119, 114)	-6.276 (± 6.2690)	-6.434 (± 5.2445)	-7.280 (± 5.8262)	

Statistical analyses

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 8.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	382
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.048
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.734
upper limit	0.638

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 16.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	382
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.431
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.367
upper limit	1.229

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 24.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	382
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.197
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.625
upper limit	1.019

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 52.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.647
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.186
upper limit	1.479

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 8.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.105
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.682
upper limit	0.891

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 16.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.245
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.667
upper limit	1.158

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 24.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.116
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.065
upper limit	0.834

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 52.

Estimated using ANCOVA model with treatment, Baseline CNV measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	382
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.156
Confidence interval	
level	Other: 2 %
sides	2-sided
lower limit	-0.561
upper limit	0.872

Secondary: Mean Change from Baseline in Central Subfield Thickness (CST)

End point title	Mean Change from Baseline in Central Subfield Thickness (CST)

End point description:

CST was defined as the average thickness in the ETDRS central 1 mm diameter subfield (the central subfield) and was measured by spectral domain optical coherence tomography.

Change from Baseline calculated as observed post-baseline value - Baseline value.

Full Analysis Set (Re-randomized): Consisted of all randomized participants, with treatment as the re-randomized treatment regardless of actual treatment received. Participants were included in the treatment group in which they were re-randomized. Analysis included participants with available data at Baseline and at each timepoint.

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 8, 16, 24, 32, 40, 48, and 52

End point values	ABP 938 / ABP 938	Aflibercept / ABP 938	Aflibercept / Aflibercept	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	273	134	136	
Units: µm				
arithmetic mean (standard deviation)				
Week 4 (n = 270, 136, 131)	-136.5 (± 108.91)	-149.7 (± 107.01)	-143.1 (± 107.32)	
Week 8 (n = 269, 134, 132)	-145.9 (± 106.24)	-167.4 (± 118.52)	-146.3 (± 110.39)	
Week 16 (n = 273, 135, 134)	-125.2 (± 124.81)	-143.2 (± 121.93)	-127.3 (± 103.35)	
Week 24 (n = 265, 133, 128)	-130.8 (± 125.63)	-151.2 (± 118.21)	-131.7 (± 102.98)	
Week 32 (n = 262, 132, 131)	-133.2 (± 122.93)	-154.8 (± 114.22)	-134.1 (± 116.02)	
Week 40 (n = 257, 130, 124)	-132.3 (± 113.25)	-155.7 (± 119.95)	-135.6 (± 119.07)	
Week 48 (n = 251, 125, 123)	-132.3 (± 124.15)	-157.8 (± 121.23)	-141.1 (± 112.29)	
Week 52 (n = 250, 125, 123)	-157.1 (± 114.25)	-177.4 (± 122.22)	-159.1 (± 108.82)	

Statistical analyses

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 16.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	1.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.9
upper limit	16.6

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 8.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11
upper limit	13.5

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 4.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	6.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.6
upper limit	17.9

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 40.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-13.7
upper limit	14.1

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 32.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-15.3
upper limit	12.9

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 24.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	0.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.1
upper limit	14.4

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 32.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-23.3
upper limit	9.3

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 40.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-6.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.8
upper limit	9.8

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 48.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-17.3
upper limit	16.2

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 24.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.6
upper limit	10.6

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 16.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-3.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-20.9
upper limit	13.3

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 8.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept

Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	-5.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-19.3
upper limit	9.1

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 4.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	6.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.4
upper limit	20

Statistical analysis title	Aflibercept/ABP 938 vs. Aflibercept/Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 52.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	Aflibercept / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	2.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.5
upper limit	15

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 48.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.4
upper limit	21.4

Statistical analysis title	ABP 938 / ABP 938 vs. Aflibercept / Aflibercept

Statistical analysis description:

Difference in mean change from Baseline at Week 52.

Estimated using ANCOVA model with treatment, Baseline CST measurement and the stratification factors geographic region (East Asia, Europe, North America) and Baseline BCVA (BCVA < 64 letters, BCVA ≥ 64 letters) as covariates.

Comparison groups	ABP 938 / ABP 938 v Aflibercept / Aflibercept
Number of subjects included in analysis	409
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference between means
Point estimate	1.6
Confidence interval	
level	Other: 2 %
sides	2-sided
lower limit	-9.3
upper limit	12.5

Secondary: Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical trial participant. TEAEs were defined as those AEs that begin or increase in severity or frequency at or after the time of first treatment to the End of Study visit. Events of interest (EOIs) pre-specified for this study included

endophthalmitis, retinal detachment, increase in intraocular pressure, and thromboembolic events. Serious AEs were defined as any untoward medical occurrence that meets at least 1 of the following serious criteria:
- Results in death
- Life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Congenital anomaly/birth defect
- Other medically important serious event.

Safety Analysis Set: Consisted of all participants who received at least 1 dose of investigational product, with treatment assignment based on actual treatment received.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Through Week 16: ABP 938	Through Week 16: Aflibercept	Post Week 16: ABP 938 / ABP 938	Post Week 16: Aflibercept / ABP 938
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	288	288	273[1]	133[2]
Units: Participants				
Any TEAEs	113	107	144	76
Any EOIs	6	3	9	8
Any Serious TEAEs	6	9	22	14

Notes:

[1] - Re-randomized and Treated.

[2] - Re-randomized and Treated.

End point values	Post Week 16: Aflibercept / Aflibercept			
Subject group type	Subject analysis set			
Number of subjects analysed	136[3]			
Units: Participants				
Any TEAEs	72			
Any EOIs	2			
Any Serious TEAEs	11			

Notes:

[3] - Re-randomized and Treated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Developing Binding Antidrug Antibodies (ADAs)

End point title	Number of Participants Developing Binding Antidrug Antibodies (ADAs)

End point description:

Number of participants with positive post-baseline ADA result through Week 16 and post Week 16 with negative or no result at Baseline is reported.

Safety Analysis Set (Re-randomized and Treated): Consisted of all participants who received at least 1 dose of investigational product, with treatment assignment based on actual treatment received. Analysis

included participants with available data at Baseline and at each timepoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	Through Week 16: ABP 938	Through Week 16: Aflibercept	Post Week 16: ABP 938 / ABP 938	Post Week 16: Aflibercept / ABP 938
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	288	288	273	133
Units: Participants	1	4	4	3

End point values	Post Week 16: Aflibercept / Aflibercept			
Subject group type	Subject analysis set			
Number of subjects analysed	136			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 52

Adverse event reporting additional description:

All-cause mortality was collected for all participants enrolled/randomized in the study. AEs were collected for all participants who received at least one dose of study drug through Week 16. AEs were collected for all participants who were re-randomized and received at least one dose of study drug post Week 16.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Through Week 16: ABP 938

Reporting group description:

Participants were treated with 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8).

Reporting group title	Through Week 16: Aflibercept

Reporting group description:

Participants were treated with 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 4 weeks for the first 3 doses (i.e., Baseline/Day 1, Week 4, and Week 8).

Reporting group title	Post Week 16: Aflibercept / Aflibercept

Reporting group description:

Participants who were initially treated with aflibercept and were re-randomized and treated with 2 mg (0.05 mL) of aflibercept by IVT injection in the study eye every 8 weeks from Week 16 until Week 48.

Reporting group title	Post Week 16: Aflibercept / ABP 938

Reporting group description:

Participants who were initially treated with aflibercept and were re-randomized and treated with 2 mg (0.05 mL) of ABP-938 by IVT injection in the study eye every 8 weeks from Week 16 until Week 48.

Reporting group title	Post Week 16: ABP 938 / ABP 938

Reporting group description:

Participants who were initially treated with ABP 938 and remained on treatment with 2 mg (0.05 mL) of ABP 938 by IVT injection in the study eye every 8 weeks from Week 16 until Week 48.

Serious adverse events	Through Week 16: ABP 938	Through Week 16: Aflibercept	Post Week 16: Aflibercept / Aflibercept
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 288 (2.08%)	9 / 288 (3.13%)	11 / 136 (8.09%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			

subjects affected / exposed	0 / 288 (0.00%)	1 / 288 (0.35%)	0 / 136 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 288 (0.00%)	1 / 288 (0.35%)	0 / 136 (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
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rosai-Dorfman syndrome			
subjects affected / exposed	1 / 288 (0.35%)	0 / 288 (0.00%)	0 / 136 (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
Squamous cell carcinoma of the tongue			

subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell cancer of the renal pelvis and ureter			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral artery stenosis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 288 (0.35%)	0 / 136 (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
Subclavian artery stenosis			
subjects affected / exposed	0 / 288 (0.00%)	1 / 288 (0.35%)	0 / 136 (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			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			

subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 288 (0.00%)	1 / 288 (0.35%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Heart rate decreased			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 288 (0.35%)	0 / 288 (0.00%)	0 / 136 (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	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ankle fracture			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 288 (0.35%)	0 / 288 (0.00%)	0 / 136 (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			
Ventricular tachycardia			
subjects affected / exposed	1 / 288 (0.35%)	0 / 288 (0.00%)	0 / 136 (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	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 288 (0.00%)	1 / 288 (0.35%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Syncope			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal haemorrhage			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual impairment			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
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 disorders			
Pneumatosis intestinalis			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Small intestinal obstruction			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
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			
Cholangitis acute			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 288 (0.35%)	0 / 288 (0.00%)	0 / 136 (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
Renal failure			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neck obstruction			
subjects affected / exposed	1 / 288 (0.35%)	0 / 288 (0.00%)	0 / 136 (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
Endocrine disorders			
Adrenal haematoma			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Haemarthrosis			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthropod-borne disease			

subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	1 / 136 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 288 (0.00%)	2 / 288 (0.69%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Appendicitis			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 288 (0.35%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 288 (0.00%)	1 / 288 (0.35%)	0 / 136 (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
Diverticulitis			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	0 / 288 (0.00%)	0 / 288 (0.00%)	0 / 136 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Post Week 16: Aflibercept / ABP 938	Post Week 16: ABP 938 / ABP 938	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 133 (10.53%)	22 / 273 (8.06%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			

subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rosai-Dorfman syndrome			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell cancer of the renal pelvis and ureter			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral artery stenosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery stenosis			

subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Heart rate decreased			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	0 / 133 (0.00%)	3 / 273 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 133 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	3 / 133 (2.26%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			

subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pneumatosis intestinalis			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis acute			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder neck obstruction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endocrine disorders			
Adrenal haematoma			
subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Haemarthrosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthropod-borne disease			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 133 (0.00%)	2 / 273 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 133 (0.75%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diverticulitis			

subjects affected / exposed	0 / 133 (0.00%)	1 / 273 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 133 (0.75%)	0 / 273 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Through Week 16: ABP 938	Through Week 16: Aflibercept	Post Week 16: Aflibercept / Aflibercept
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 288 (6.25%)	15 / 288 (5.21%)	17 / 136 (12.50%)
Eye disorders			
Neovascular age-related macular degeneration			
subjects affected / exposed	6 / 288 (2.08%)	4 / 288 (1.39%)	11 / 136 (8.09%)
occurrences (all)	6	4	11
Conjunctival haemorrhage			
subjects affected / exposed	12 / 288 (4.17%)	11 / 288 (3.82%)	8 / 136 (5.88%)
occurrences (all)	15	13	10

Non-serious adverse events	Post Week 16: Aflibercept / ABP 938	Post Week 16: ABP 938 / ABP 938	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 133 (12.78%)	20 / 273 (7.33%)	

Eye disorders			
Neovascular age-related macular degeneration			
subjects affected / exposed	10 / 133 (7.52%)	16 / 273 (5.86%)	
occurrences (all)	10	16	
Conjunctival haemorrhage			
subjects affected / exposed	8 / 133 (6.02%)	4 / 273 (1.47%)	
occurrences (all)	11	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 October 2019	Amendment 1: - Inclusion Criteria was updated. - Exclusion Criteria was updated. - Fundus photography was added as an efficacy assessment.
23 March 2021	Amendment 2: - Non-Amgen Investigational Product (Aflibercept) was updated to include additional adverse events reflected in the warnings and precautions section of the product labeling. - Benefit/Risk Assessment was updated to include a COVID-19 risk assessment. - Study Objective and Endpoints, 1 of the secondary efficacy endpoints was updated. - Study Design was updated to include information on the pharmacokinetic substudy and treatment of the fellow eye. - Inclusion Criteria was updated. - Exclusion Criteria was updated. - Antidrug Antibodies was updated. - Treatment of the Fellow Eye was updated. - A new section, Coronavirus Disease 2019 Considerations was included.
16 May 2022	Amendment 3: - Study Objectives, Endpoints, and Estimand was updated to include the information of primary estimand. - Primary Endpoint/Estimand was updated to include the analysis of primary estimand.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported