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Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Brolucizumab (RTH258)

Trial Indication(s)

Visual impairment due to diabetic macular edema (DME)

Protocol Number

CRTH258B2302

Protocol Title

A Two-Year, Two-Arm, Randomized, Double Masked, Multicenter, Phase III Study Assessing the Efficacy and Safety of Brolucizumab versus Aflibercept in Adult Patients with Visual Impairment due to Diabetic Macular Edema

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: July 2018 (Actual)
Primary Completion Date: June 2020 (Actual)
Study Completion Date: June 2021 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a Phase III, randomized, double-masked, multi-center, active-controlled, two-arm study designed to evaluate the efficacy and safety of brolucizumab 6 mg compared to the active control, aflibercept 2 mg used per authorized label, in subjects with DME. The study included a screening period of up to 2 weeks to assess eligibility, followed by a double-masked treatment period (Day 1 to Week 96). The baseline visit was defined as Day 1/Visit 1, and end of treatment visit as Visit 27 (Week 96). After the last treatment visit, there was a post-treatment follow-up period from Week 96 to Week 100 and an exit visit at Week 100.

Subjects were assigned to one of two treatment arms in a 1:1 ratio: brolucizumab 6 mg/0.05 mL administered 5 x every 6 weeks (q6w) during loading phase then q12w/q8w during maintenance phase with an option to extend treatment interval by 4 weeks at Week 72 during the second year or aflibercept 2 mg/0.05 mL administered 5 x every 4 weeks (q4w) during loading phase then q8w during maintenance phase through Week 96.

Disease activity assessments (DAAs) were conducted by the masked investigator for both treatment arms at Week 32 and Week 36, i.e., 8 and 12 weeks after the end of the loading phase for subjects receiving brolucizumab, and at Week 48, Week 60 and Week 72 (i.e., every 12 weeks). In the brolucizumab arm, subjects who qualified for q12w during this initial q12w interval (i.e., at Week 32 and Week 36) continued on a q12w treatment frequency unless disease activity was identified at any of the subsequent DAA visits, in which case subjects were switched to a q8w treatment interval until Week 72.

A one-time disease stability assessment was performed by the masked investigator at Week 72 in both treatment arms with the purpose of evaluating the potential for treatment interval extension by 4 weeks. The subjects in the brolucizumab arm who demonstrated disease stability in the one-time assessment at Week 72 under their current assigned treatment regimen (q12w or q8w) were considered for treatment interval extension (i.e., q12w to q16w or q8w to q12w). To evaluate the adequacy of the individualized q8w, q12w or q16w treatment intervals in the brolucizumab arm, DAAs were performed at every visit from Week 72 up to and including Week 96 (i.e., every 4 weeks). If after Week 72 disease activity had been identified by the masked investigator, the subjects' treatment interval was revealed to q8w at their next scheduled treatment visit (according to the subject's specific treatment schedule q12w or q16w) and the q8w interval was remained through Week 96.

Centers

79 centers in 23 countries: Czech Republic(3), Turkey(5), Belgium(1), Korea, Republic of(6), France(12), Singapore(2), Switzerland(2), Latvia(1), Lithuania(2), Germany(7), Hungary(5), Taiwan(3), Malaysia(2), Slovakia (Slovak Republic)(5), Denmark(2), Norway(1), Estonia(2), Lebanon(3), Sweden(1), Russia(5), India(5), Bulgaria(3), Poland(1)

Objectives:

The primary and secondary objectives for this study are presented below along with their respective endpoints.

Objective(s)	Endpoint(s)
Primary objective	**Endpoint for primary objective**
To demonstrate that brolucizumab is non-inferior to aflibercept with respect to the visual outcome after the first year of treatment	● Change from baseline in best-corrected visual acuity (BCVA) at Week 52
Secondary objective(s)	**Endpoint(s) for secondary objective(s)**
To demonstrate that brolucizumab is non-inferior to aflibercept with respect to visual outcome during the last 3 months of the first year of treatment	● Change from baseline in BCVA averaged over a period Week 40 to Week 52
To estimate the proportion of patients treated at every 12 weeks (q12w) frequency with brolucizumab	● Proportion of patients maintained at q12w up to Week 52 & 100
To estimate the predictive value of the first q12w cycle for maintenance of q12w treatment with brolucizumab	● Proportion of patients maintained at q12w up to Week 52, within those patients that qualified for q12w at Week 36 ● Proportion of patients maintained at q12w/ every 16 weeks (q16w) up to Week 100, within those patients that qualified for q12w at Week 36

Objective(s)	Endpoint(s)
To assess the potential to extend treatment intervals for brolucizumab patients during the second year of treatment	● Proportion of patients maintained on q16w up to Week 100 within the patients on q12w at Week 68 and on q16w at Week 76 ● Proportion of patients re-assigned and maintained on q12w up to Week 100 within the patients on every 8 weeks (q8w) at Week 68 and on q12w at Week 80 ● Treatment status at Week 100
To evaluate the functional and anatomical outcome with brolucizumab relative to aflibercept	● Change from baseline by visit up to Week 100 in BCVA and in parameters derived from spectral domain optical coherence tomography (SD-OCT), color fundus photography and fluorescein angiography
To evaluate the effect of brolucizumab relative to aflibercept on the diabetic retinopathy (DR) status	● Change in Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale (DRSS) score up to Week 100
To assess the safety of brolucizumab relative to aflibercept	● Incidence of ocular and non-ocular adverse events (AEs), vital signs and laboratory values up to Week 100
To evaluate the effect of brolucizumab relative to aflibercept on patient-reported outcomes (Visual Functioning Questionnaire-25 [VFQ-25])	● Change in patient reported outcomes (VFQ-25) total and subscale scores from baseline up to Week 100
To confirm the systemic brolucizumab exposure in patients with visual impairment due to diabetic macular edema (DME)	● Systemic brolucizumab concentration approximately 24 hours after initial and final loading phase doses
To assess the immunogenicity of brolucizumab over two years of treatment	● Anti-drug antibody (ADA) status at baseline and up to Week 100

Test Product (s), Dose(s), and Mode(s) of Administration

The investigational treatment brolucizumab was provided in a sterile glass vial for single use containing 6 mg/0.05 mL (or

in prefilled syringe in selected countries).
The comparator treatment aflibercept was provided in a sterile glass vial for single use containing 2 mg/0.05 mL (or any other marketed presentation available).

Statistical Methods

The objectives related to the primary and first key secondary endpoints were to demonstrate non-inferiority of brolucizumab to aflibercept with respect to the change from baseline in BCVA at Week 52 and over a period Week 40 to Week 52, respectively, considering a margin of 4 ETDRS letters. The non-inferiority of brolucizumab vs. aflibercept was analyzed by testing the following non-inferiority hypotheses related to a non-inferiority margin of 4 letters via an analysis of variance (ANOVA) model:

- H_{01}: $\mu_B - \mu_A \leq$ -4 letters vs. H_{A1}: $\mu_B - \mu_A >$ -4 letters
- H_{02}: $\varphi_B - \varphi_A \leq$ -4 letters vs. H_{A2}: $\varphi_B - \varphi_A >$ -4 letters

where B = Brolucizumab 6 mg administered 5 x q6w during loading phase then q12w/q8w during maintenance phase, A = Aflibercept 2 mg administered 5 x q4w during loading phase then q8w during maintenance phase; μ_B and μ_A were the corresponding unknown true mean changes from baseline in BCVA at Week 52 in the brolucizumab and aflibercept arms, respectively; φ_B and φ_A were the corresponding unknown true mean changes from baseline in BCVA averaged over the period Week 40 to Week 52 in the brolucizumab and aflibercept arms, respectively.

The model included treatment, baseline BCVA (=< 65, > 65 letters) and age category (< 65, >= 65 years) as factors. Two-sided 95% confidence interval (CI) for the least-square (LS) mean difference (brolucizumab - aflibercept) were presented in letters. Non-inferiority was considered established if the lower limit of the corresponding 95% CI was greater than -4 letters. P-value for treatment comparison (two-sided) and p-value for non-inferiority (4-letter margin) (one-sided) were presented. The two alternative hypotheses (H_{A1}, H_{A2}) were tested sequentially in the order of their numbering, i.e., confirmatory testing of the second hypothesis required rejection of the first null hypothesis. In this setting, each hypothesis was assessed at a one-sided significance level of 0.025, while keeping the global type I error rate at 0.025.

No statistical hypotheses were tested for the additional key secondary efficacy endpoints (proportion of subjects maintained at q12w up to Week 52 and proportion of subjects maintained at q12w up to Week 52, within those subjects that qualified for q12w at Week 36). The proportion of subjects with a positive q12w treatment status at Week 52 was presented together

with two-sided 95% CIs. The outcome of the Kaplan-Meier analysis was presented graphically by the estimated q12w-probability over time, i.e., at each DAA visit.

The secondary endpoints related to BCVA, dosing regimen (q8w treatment need status), anatomy (CSFT, SRF and IRF status, presence of leakage on fluorescein angiography) and status of DR were summarized and presented descriptively, based on the Full analysis set with last observation carried forward (LOCF) imputation for missing data and LOCF replacement for censored data.

Superiority testing of hypotheses for additional secondary endpoints was performed on the condition that proof of non-inferiority related to BCVA was successful for the two hypotheses (H_1 and H_2) specified for the primary and first key secondary endpoints. All tests were one-sided tests for superiority of brolucizumab vs. aflibercept on the additional efficacy hypotheses linked to the following endpoints:

- H_3. Average change from baseline in CSFT over the period Week 40 through Week 52 in the study eye;
- H_4. Average change from baseline in BCVA over the period Week 40 through Week 52 in the study eye;
- H_5. Fluid-status 'yes/no' in the study eye at Week 52 (no=absence of SRF and IRF).

The alternative hypotheses were to be tested hierarchically in the order H_3, then H_4, then H_5, i.e., confirmatory testing of the hypothesis required rejection of the previous null hypothesis. In this setting, each hypothesis was assessed at a one-sided significance level of 0.025, while keeping the global type I error rate at 0.025.

The proportion of subjects with q12w/q16w treatment status was presented together with two-sided 95% CIs. The outcome of the Kaplan-Meier analysis was presented graphically by the estimated q12w/q16w-probability over time, i.e., at each DAA visit.

The secondary endpoints related to BCVA, dosing regimen (q8w treatment need status at each DAA visit and treatment status at Week 100 of the subjects who completed the study treatment period), anatomy (CSFT, SRF and IRF status, presence of leakage on fluorescein angiography) and status of DR were summarized and presented descriptively, based on the Full analysis set with last observation carried forward (LOCF) imputation for missing data and LOCF replacement for censored data.

The safety analyses were descriptive, no hypothesis testing was performed. Treatment-emergent ocular and non-ocular AEs were summarized by treatment arm. ADA integrated status and positive neutralized antibody (NAb), as well as the incidence of AESIs by ADA were summarized for subjects in the brolucizumab arm.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:
General
• Patients must give written informed consent before any study related assessments are performed
• Patients with type 1 or type 2 diabetes mellitus and HbA1c of =< 10% at screening
• Medication for the management of diabetes must have been stable within 3 months prior to randomization and is expected to remain stable during the course of the study

Study Eye
• Visual impairment due to DME with:
a) BCVA score between 78 and 23 letters, inclusive, using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at a testing distance of 4 meters (approximate Snellen equivalent of 20/32 to 20/320), at screening and baseline
b) DME involving the center of the macula, with central subfield retinal thickness (measured from RPE to ILM inclusively) of >= 320 micrometers (µm) on SD-OCT at screening
If both eyes are eligible, the eye with the worse visual acuity will be selected for study eye. However, the investigator may select the eye with better visual acuity, based on medical reasons or local ethical requirements.

Key Exclusion Criteria:
• Previous treatment with any anti-VEGF drugs or investigational drugs in the study eye
• Active proliferative diabetic retinopathy in the study eye as per the investigator
• Concomitant conditions or ocular disorders in the study eye at screening or baseline which could, in the opinion of the investigator, prevent response to study treatment or may confound interpretation of study results, compromise visual acuity or require medical or surgical intervention during the first 12-month study period (e.g., cataract, vitreous hemorrhage, retinal vascular occlusion, retinal detachment, macular hole, or choroidal neovascularization of any cause)
• Any active intraocular or periocular infection or active intraocular inflammation (e.g., infectious conjunctivitis, keratitis, scleritis, endophthalmitis, infectious blepharitis, uveitis) in study eye at screening or baseline
• Structural damage of the fovea in the study eye at screening likely to preclude improvement in visual acuity following the resolution of macular edema, including atrophy of the retinal pigment epithelium, subretinal fibrosis, laser scar(s), epiretinal membrane involving fovea or organized hard exudate plaques
• Uncontrolled glaucoma in the study eye defined as intraocular pressure (IOP) > 25 millimeters mercury (mmHg) on medication or according to investigator’s judgment, at screening or baseline
• Neovascularization of the iris in the study eye at screening or baseline
• Evidence of vitreomacular traction in the study eye at screening or baseline which, in the opinion of the investigator, affect visual

acuity

Participant Flow Table

Overall Study

	Brolucizumab 6 mg	Aflibercept 2 mg	Total
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks	
Started	179	181	360
Completed	143	156	299
Not Completed	36	25	61
Adverse Event	5	4	9
Death	13	9	22
Lost to Follow-up	2	2	4
Physician Decision	2	3	5
Withdrawal by Subject	14	7	21

Baseline Characteristics

	Brolucizumab 6 mg	Aflibercept 2 mg	Total
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks	
Number of Participants [units: participants]	179	181	360
Age, Customized (units: Participants)			

< 65 years	100	102	202
>= 65 years	79	79	158
Age Continuous (units: Years) Mean ± Standard Deviation			
	62.3±10.55	62.2±9.48	62.2±10.01
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)			
Female	59	66	125
Male	120	115	235
Race (NIH/OMB) (units: Participants) Count of Participants (Not Applicable)			
American Indian or Alaska Native	0	0	0
Asian	43	48	91
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	1	4
White	133	132	265
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) (units: Participants) Count of Participants (Not Applicable)			
Hispanic or Latino	3	4	7
Not Hispanic or Latino	163	170	333
Unknown or Not Reported	13	7	20

Primary Outcome Result(s)

Mean change from Baseline in best-corrected visual acuity (BCVA) at Week 52 for the study eye

(Time Frame: Baseline, Week 52)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Mean change from Baseline in best-corrected visual acuity (BCVA) at Week 52 for the study eye (units: Scores on a scale) Least Squares Mean (95% Confidence Interval)		
	10.6 (9.3 to 11.9)	9.4 (8.1 to 10.7)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA at Week 52
Non-Inferiority/Equivalence Test	Non-Inferiority	(4-letter margin) (1-sided)
P Value	<0.001	
Method	ANOVA	
Other LS mean difference	1.2	
Standard Error of the mean	0.94	

95 % Confidence Interval 2-Sided	-0.6 to 3.1

Secondary Outcome Result(s)

Average mean change from Baseline in BCVA over the period Week 40 through Week 52 for the study eye

(Time Frame: Baseline, period Week 40 through Week 52)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Average mean change from Baseline in BCVA over the period Week 40 through Week 52 for the study eye (units: Scores on a scale) Least Squares Mean (95% Confidence Interval)		
	10.3 (9.1 to 11.5)	9.4 (8.2 to 10.6)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 40 through Week 52
Non-Inferiority/Equivalence Test	Non-Inferiority	(4-letter margin) (1-sided)
P Value	<0.001	
Method	ANOVA	

Other LS mean difference	0.9
Standard Error of the mean	0.88
95 % Confidence Interval 2-Sided	-0.9 to 2.6

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 40 through Week 52
P Value	0.164	
Method	ANOVA	

(Brolucizumab treatment arm only): Percentage of participants maintained at q12w up to Week 52 and up to q12w/q16w up to Week 100.

(Time Frame: Week 52, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	0
(Brolucizumab treatment arm only): Percentage of participants maintained at q12w up to Week 52 and up to q12w/q16w up to Week 100. (units: Percentage of participants) Number (95% Confidence Interval)		
Week 48	50.3 (42.5 to 57.7)	
Week 96	36.8 (29.1 to 45.5)	

(Brolucizumab treatment arm only): Percentage of participants maintained at q12w up to Week 52 within those patients that qualified for q12w at Week 36

(Time Frame: Week 36, Week 52)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	87	0
(Brolucizumab treatment arm only): Percentage of participants maintained at q12w up to Week 52 within those patients that qualified for q12w at Week 36 (units: Percentage of participants) Number (95% Confidence Interval)		
Week 48	95.1 (87.4 to 98.1)	

(Brolucizumab treatment arm only): Percentage of participants maintained at q12w/q16w up to Week 100, within those patients that qualified for q12w at Week 36

(Time Frame: Week 36, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	87	0
(Brolucizumab treatment arm only): Percentage of participants maintained at q12w/q16w up to Week 100, within those patients that		

qualified for q12w at Week 36 (units: Percentage of participants) Number (95% Confidence Interval)	
Week 100	69.6 (57.4 to 78.9)

(Brolucizumab treatment arm only): Percentage of participants maintained on q16w up to Week 100 within the patients on q12w at Week 68 and on q16w at Week 76

(Time Frame: Week 68, Week 76, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	44	0
(Brolucizumab treatment arm only): Percentage of participants maintained on q16w up to Week 100 within the patients on q12w at Week 68 and on q16w at Week 76 (units: Percentage of participants) Number (95% Confidence Interval)		
Week 100	87.9 (73.3 to 94.8)	

(Brolucizumab treatment arm only): Percentage of participants re-assigned and maintained on q12w up to Week 100 within the patients on q8w at Week 68 and on q12w at Week 80

(Time Frame: Week 68, Week 80, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	34	0
(Brolucizumab treatment arm only): Percentage of participants re-assigned and maintained on q12w up to Week 100 within the patients on q8w at Week 68 and on q12w at Week 80 (units: Percentage of participants) Number (95% Confidence Interval)		
Week 100	73.1 (54.5 to 85.0)	

(Brolucizumab treatment arm only): Number of participants with injections per planned dosing regimen (every 8, 12 or 16 weeks)

(Time Frame: Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	141	0
(Brolucizumab treatment arm only): Number of participants with injections per planned dosing regimen (every 8, 12 or 16 weeks) (units: Participants)		

Count of Participants (Not Applicable)		
q8w	74 (52.48%)	(NaN%)
q12w	32 (22.7%)	(NaN%)
q16w	35 (24.82%)	(NaN%)

Mean change from Baseline in Best Corrected Visual Acuity (BCVA) at each visit up to Week 100 for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Mean change from Baseline in Best Corrected Visual Acuity (BCVA) at each visit up to Week 100 for the study eye (units: Scores on a scale) Least Squares Mean (95% Confidence Interval)		
Week 4	5.1 (4.3 to 6.0)	4.2 (3.4 to 5.1)
Week 6	6.8 (5.9 to 7.6)	5.9 (5.0 to 6.7)
Week 8	7.8 (6.9 to 8.7)	6.7 (5.8 to 7.5)
Week 12	8.6 (7.6 to 9.5)	7.7 (6.7 to 8.6)
Week 16	9.0 (7.9 to 10.1)	8.3 (7.2 to 9.5)
Week 18	9.2 (8.0 to 10.3)	9.2 (8.0 to 10.3)

Week 20	9.6 (8.4 to 10.8)	9.4 (8.2 to 10.6)
Week 24	10.0 (8.8 to 11.2)	8.7 (7.5 to 9.9)
Week 28	9.8 (8.6 to 11.1)	9.4 (8.2 to 10.6)
Week 32	10.3 (9.1 to 11.5)	8.9 (7.7 to 10.1)
Week 36	9.6 (8.4 to 10.9)	9.4 (8.2 to 10.7)
Week 40	9.9 (8.7 to 11.2)	9.2 (7.9 to 10.4)
Week 44	10.6 (9.3 to 11.8)	9.5 (8.3 to 10.8)
Week 48	10.1 (8.8 to 11.3)	9.6 (8.3 to 10.9)
Week 52	10.6 (9.3 to 11.9)	9.4 (8.1 to 10.7)
Week 56	10.7 (9.3 to 12.0)	9.5 (8.2 to 10.9)
Week 60	10.5 (9.1 to 11.9)	9.3 (8.0 to 10.7)
Week 64	11.0 (9.7 to 12.3)	9.5 (8.2 to 10.8)
Week 68	11.0 (9.6 to 12.3)	9.5 (8.2 to 10.8)
Week 72	11.0 (9.6 to 12.3)	9.4 (8.1 to 10.8)
Week 76	10.5 (9.2 to 11.8)	9.8 (8.4 to 11.1)
Week 80	10.2 (8.9 to 11.6)	9.4 (8.1 to 10.8)

Week 84	10.9 (9.4 to 12.4)	8.9 (7.4 to 10.4)
Week 88	10.7 (9.1 to 12.4)	8.6 (7.0 to 10.2)
Week 92	10.7 (9.1 to 12.2)	9.3 (7.7 to 10.8)
Week 96	10.7 (9.1 to 12.3)	8.5 (6.8 to 10.1)
Week 100	10.9 (9.3 to 12.6)	8.4 (6.7 to 10.1)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment Difference
Other LS mean difference	1.2	
Standard Error of the mean	0.94	
95 % Confidence Interval 2-Sided	-0.6 to 3.1	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment Difference
Other LS mean difference	2.6	
Standard Error of the mean	1.21	

95 % Confidence Interval 2-Sided	0.2 to 4.9

Average mean change from Baseline in Best Corrected Visual Acuity (BCVA) over the period Week 4 to Week 52/100 for the study eye

(Time Frame: Baseline, period Week 4 through Week 52, period Week 4 through Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Average mean change from Baseline in Best Corrected Visual Acuity (BCVA) over the period Week 4 to Week 52/100 for the study eye (units: Scores on a scale) Least Squares Mean (95% Confidence Interval)		
period Week 4 through Week 52	9.1 (8.2 to 10.1)	8.4 (7.4 to 9.3)
period Week 4 through Week 100	9.8 (8.8 to 10.9)	8.7 (7.7 to 9.8)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 4 through Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	0.8	
Standard Error of the mean	0.70	
95 % Confidence Interval 2-Sided	-0.6 to 2.1	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 4 through Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	1.1	
Standard Error of the mean	0.78	
95 % Confidence Interval 2-Sided	-0.4 to 2.6	

Average mean change from Baseline in Best Corrected Visual Acuity (BCVA) over the period Week 20 to Week 52/100 and Week 28 to Week 52/100 for the study eye

(Time Frame: Baseline, period Week 20 through Week 52, period Week 20 through Week 100, period Week 28 through Week 52, period Week 28 through Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Average mean change from Baseline in Best Corrected Visual Acuity (BCVA) over the period Week 20 to Week 52/100 and Week 28 to Week 52/100 for the study eye (units: Scores on a scale) Least Squares Mean (95% Confidence Interval)		
period Week 20 through Week 52	10.1 (8.9 to 11.2)	9.3 (8.1 to 10.4)
period Week 20 through Week 100	10.4 (9.2 to 11.7)	9.2 (8.0 to 10.4)
period Week 28 through Week 52	10.1 (9.0 to 11.3)	9.4 (8.2 to 10.5)
period Week 28 through Week 100	10.5 (9.3 to 11.7)	9.2 (8.0 to 10.5)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 20 through Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	0.8	
Standard Error of the mean	0.83	
95 % Confidence Interval 2-Sided	-0.9 to 2.4	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 28 through Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	0.8	
Standard Error of the mean	0.85	
95 % Confidence Interval 2-Sided	-0.9 to 2.5	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 20 through Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	1.2	
Standard Error of the mean	0.87	

95 % Confidence Interval 2-Sided	-0.5 to 2.9

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 28 through Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	1.3	
Standard Error of the mean	0.89	
95 % Confidence Interval 2-Sided	-0.5 to 3.0	

Average mean change from Baseline in Best Corrected Visual Acuity (BCVA) over the period Week 88 to 100 for the study eye

(Time Frame: Baseline, period Week 88 through Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Average mean change from Baseline in Best Corrected Visual Acuity (BCVA) over the period Week 88 to 100 for the study eye (units: Scores on a scale) Least Squares Mean (95% Confidence Interval)		
	10.8 (9.2 to 12.3)	8.7 (7.1 to 10.2)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	BCVA over period Week 88 through Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	2.1	
Standard Error of the mean	1.12	
95 % Confidence Interval 2-Sided	-0.1 to 4.3	

Percentage of participants who gained >= 5 letters in BCVA from Baseline or reached BCVA >= 84 letters at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants who gained >= 5 letters in BCVA from Baseline or reached BCVA >= 84 letters at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	49.2 (41.6 to 56.7)	46.4 (39.0 to 54.0)
Week 6	62.0 (54.5 to 69.1)	62.4 (54.9 to 69.5)
Week 8	67.6 (60.2 to 74.4)	63.5 (56.1 to 70.5)

Week 12	70.9 (63.7 to 77.5)	73.5 (66.4 to 79.8)
Week 16	71.5 (64.3 to 78.0)	73.5 (66.4 to 79.8)
Week 18	77.7 (70.8 to 83.5)	77.9 (71.1 to 83.7)
Week 20	79.3 (72.7 to 85.0)	76.2 (69.4 to 82.2)
Week 24	79.9 (73.3 to 85.5)	77.9 (71.1 to 83.7)
Week 28	75.4 (68.4 to 81.5)	77.9 (71.1 to 83.7)
Week 32	77.1 (70.2 to 83.0)	80.7 (74.1 to 86.1)
Week 36	74.3 (67.2 to 80.5)	80.7 (74.1 to 86.1)
Week 40	74.9 (67.8 to 81.0)	79.6 (72.9 to 85.2)
Week 44	74.3 (67.2 to 80.5)	80.7 (74.1 to 86.1)
Week 48	76.0 (69.0 to 82.0)	79.0 (72.3 to 84.7)
Week 52	77.7 (70.8 to 83.5)	79.0 (72.3 to 84.7)
Week 56	77.7 (70.8 to 83.5)	80.7 (74.1 to 86.1)
Week 60	76.0 (69.0 to 82.0)	79.0 (72.3 to 84.7)
Week 64	78.2 (71.4 to 84.0)	79.0 (72.3 to 84.7)
Week 68	77.7 (70.8 to 83.5)	76.8 (70.0 to 82.7)

Week 72	79.9 (73.3 to 85.5)	77.3 (70.6 to 83.2)
Week 76	74.3 (67.2 to 80.5)	77.3 (70.6 to 83.2)
Week 80	74.3 (67.2 to 80.5)	75.7 (68.8 to 81.7)
Week 84	78.2 (71.4 to 84.0)	73.5 (66.4 to 79.8)
Week 88	77.7 (70.8 to 83.5)	75.7 (68.8 to 81.7)
Week 92	79.3 (72.7 to 85.0)	74.0 (67.0 to 80.3)
Week 96	78.8 (72.0 to 84.5)	73.5 (66.4 to 79.8)
Week 100	77.1 (70.2 to 83.0)	73.5 (66.4 to 79.8)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Gain of >= 5 letters in BCVA at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	0.4	
95 % Confidence Interval 2-Sided	-7.6 to 8.9	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Gain of >= 5 letters in BCVA at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference

Other Clopper-Pearson exact method	5.4
95 % Confidence Interval 2-Sided	-3.9 to 14.5

Percentage of participants who gained >= 10 letters in BCVA from Baseline or reached BCVA >= 84 letters at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants who gained >= 10 letters in BCVA from Baseline or reached BCVA >= 84 letters at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	22.9 (17.0 to 29.8)	23.8 (17.8 to 30.6)
Week 6	34.6 (27.7 to 42.1)	31.5 (24.8 to 38.8)
Week 8	39.7 (32.4 to 47.2)	36.5 (29.5 to 43.9)
Week 12	43.0 (35.7 to 50.6)	45.9 (39.4 to 53.4)
Week 16	44.1 (36.7 to 51.7)	49.7 (42.2 to 57.2)
Week 18	47.5 (40.0 to 55.1)	53.0 (45.5 to 60.5)
Week 20	53.1 (45.5 to 60.6)	56.9 (49.4 to 64.2)

Week 24	56.4 (48.8 to 63.8)	53.6 (46.0 to 61.0)
Week 28	55.3 (47.7 to 62.7)	55.2 (47.7 to 62.6)
Week 32	58.7 (51.1 to 66.0)	51.9 (44.4 to 59.4)
Week 36	57.5 (49.9 to 64.9)	55.2 (47.7 to 62.6)
Week 40	58.1 (50.5 to 65.4)	52.5 (44.9 to 59.9)
Week 44	61.5 (53.9 to 68.6)	56.9 (49.4 to 64.2)
Week 48	60.9 (53.3 to 68.1)	53.0 (45.5 to 60.5)
Week 52	61.5 (53.9 to 68.6)	58.6 (51.0 to 65.8)
Week 56	62.0 (54.5 to 69.1)	54.1 (46.6 to 61.6)
Week 60	61.5 (53.9 to 68.6)	54.7 (47.1 to 62.1)
Week 64	63.7 (56.2 to 70.7)	56.9 (49.4 to 64.2)
Week 68	62.0 (54.5 to 69.1)	57.5 (49.9 to 64.8)
Week 72	63.7 (56.2 to 70.7)	56.4 (48.8 to 63.7)
Week 76	60.9 (53.3 to 68.1)	56.9 (49.4 to 64.2)
Week 80	57.5 (49.9 to 64.9)	55.8 (48.2 to 63.2)
Week 84	63.7 (56.2 to 70.7)	58.6 (51.0 to 65.8)

Week 88	61.5 (53.9 to 68.6)	58.0 (50.5 to 65.3)
Week 92	63.7 (56.2 to 70.7)	58.6 (51.0 to 65.8)
Week 96	62.6 (55.0 to 69.7)	56.9 (49.4 to 64.2)
Week 100	61.5 (53.9 to 68.6)	54.1 (46.6 to 61.6)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Gain of >= 10 letters in BCVA at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	5.4	
95 % Confidence Interval 2-Sided	-3.9 to 14.7	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Gain of >= 10 letters in BCVA at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	9.9	
95 % Confidence Interval 2-Sided	-0.4 to 19.4	

Percentage of participants who gained >= 15 letters in BCVA from Baseline or reached BCVA >= 84 letters at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants who gained >= 15 letters in BCVA from Baseline or reached BCVA >= 84 letters at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	12.3 (7.9 to 18.0)	9.4 (5.6 to 14.6)
Week 6	13.4 (8.8 to 19.3)	13.8 (9.1 to 19.7)
Week 8	25.1 (19.0 to 32.2)	16.0 (11.0 to 22.2)
Week 12	25.1 (19.0 to 32.2)	22.1 (16.3 to 28.9)
Week 16	33.5 (26.7 to 40.9)	25.4 (19.2 to 32.4)
Week 18	31.8 (25.1 to 39.2)	33.1 (26.3 to 40.5)
Week 20	34.6 (27.7 to 42.1)	32.6 (25.8 to 39.9)
Week 24	41.9 (34.6 to 49.5)	30.9 (24.3 to 38.2)
Week 28	40.2 (33.0 to 47.8)	37.0 (30.0 to 44.5)
Week 32	44.1 (36.7 to 51.7)	30.4 (23.8 to 37.6)

Week 36	45.3 (37.8 to 52.8)	32.6 (25.8 to 39.9)
Week 40	44.7 (37.3 to 52.3)	31.5 (24.8 to 38.8)
Week 44	50.3 (42.7 to 57.8)	35.4 (28.4 to 42.8)
Week 48	41.9 (34.6 to 49.5)	37.0 (30.0 to 44.5)
Week 52	46.4 (38.9 to 54.0)	37.6 (30.5 to 45.1)
Week 56	46.4 (38.9 to 54.0)	35.9 (28.9 to 43.4)
Week 60	46.9 (39.4 to 54.5)	38.7 (31.5 to 46.2)
Week 64	50.3 (42.7 to 57.8)	36.5 (29.5 to 43.9)
Week 68	48.6 (41.1 to 56.2)	35.9 (28.9 to 43.4)
Week 72	48.0 (40.5 to 55.6)	35.4 (28.4 to 42.8)
Week 76	46.4 (38.9 to 54.0)	40.9 (33.6 to 48.4)
Week 80	43.6 (36.2 to 51.2)	37.6 (30.5 to 45.1)
Week 84	46.4 (38.9 to 54.0)	37.0 (30.0 to 44.5)
Week 88	47.5 (40.0 to 55.1)	40.9 (33.6 to 48.4)
Week 92	44.7 (37.3 to 52.3)	40.3 (33.1 to 47.9)
Week 96	46.9 (39.4 to 54.5)	38.1 (31.0 to 45.6)

Week 100	49.7 (42.2 to 57.3)	37.6 (30.5 to 45.1)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Gain of >= 15 letters in BCVA at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	9.6	
95 % Confidence Interval 2-Sided	-0.4 to 20.2	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Gain of >= 15 letters in BCVA at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	13.6	
95 % Confidence Interval 2-Sided	3.3 to 23.5	

Percentage of participants who lost >= 5 ETDRS letters in Best Corrected Visual Acuity (BCVA) from Baseline at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks

Number of Participants Analyzed [units: participants]	179	181
Percentage of participants who lost >= 5 ETDRS letters in Best Corrected Visual Acuity (BCVA) from Baseline at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	3.4 (1.2 to 7.2)	4.4 (1.9 to 8.5)
Week 6	1.7 (0.3 to 4.8)	3.3 (1.2 to 7.1)
Week 8	1.1 (0.1 to 4.0)	2.8 (0.9 to 6.3)
Week 12	1.1 (0.1 to 4.0)	2.2 (0.6 to 5.6)
Week 16	0.6 (0.0 to 3.1)	2.2 (0.6 to 5.6)
Week 18	1.1 (0.1 to 4.0)	1.1 (0.1 to 3.9)
Week 20	2.2 (0.6 to 5.6)	2.8 (0.9 to 6.3)
Week 24	1.7 (0.3 to 4.8)	3.3 (1.2 to 7.1)
Week 28	1.7 (0.3 to 4.8)	2.2 (0.6 to 5.6)
Week 32	2.2 (0.6 to 5.6)	2.2 (0.6 to 5.6)
Week 36	4.5 (1.9 to 8.6)	1.1 (0.1 to 3.9)
Week 40	3.9 (1.6 to 7.9)	2.2 (0.6 to 5.6)
Week 44	2.8 (0.9 to 6.4)	2.2 (0.6 to 5.6)

Week 48	2.8 (0.9 to 6.4)	2.8 (0.9 to 6.3)
Week 52	3.4 (1.2 to 7.2)	3.3 (1.2 to 7.1)
Week 56	5.0 (2.3 to 9.3)	3.3 (1.2 to 7.1)
Week 60	3.9 (1.6 to 7.9)	4.4 (1.9 to 8.5)
Week 64	2.8 (0.9 to 6.4)	3.3 (1.2 to 7.1)
Week 68	3.9 (1.6 to 7.9)	2.8 (0.9 to 6.3)
Week 72	4.5 (1.9 to 8.6)	5.0 (2.3 to 9.2)
Week 76	3.4 (1.2 to 7.2)	4.4 (1.9 to 8.5)
Week 80	2.8 (0.9 to 6.4)	6.1 (3.1 to 10.6)
Week 84	3.4 (1.2 to 7.2)	7.7 (4.3 to 12.6)
Week 88	3.9 (1.6 to 7.9)	7.2 (3.9 to 12.0)
Week 92	3.4 (1.2 to 7.2)	6.6 (3.5 to 11.3)
Week 96	3.9 (1.6 to 7.9)	7.2 (3.9 to 12.0)
Week 100	2.8 (0.9 to 6.4)	8.3 (4.7 to 13.3)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Loss of >= 5 letters in BCVA at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-0.4	
95 % Confidence Interval 2-Sided	-4.2 to 2.9	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Loss of >= 5 letters in BCVA at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-6.0	
95 % Confidence Interval 2-Sided	-10.8 to -1.7	

Percentage of participants who lost >= 10 ETDRS letters in Best Corrected Visual Acuity (BCVA) from Baseline at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants who lost >= 10 ETDRS letters in Best Corrected Visual Acuity (BCVA) from Baseline at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		

Week 4		1.1 (0.1 to 3.9)
Week 6	1.1 (0.1 to 4.0)	0.6 (0.0 to 3.0)
Week 8	1.1 (0.1 to 4.0)	
Week 12		0.6 (0.0 to 3.0)
Week 16	0.6 (0.0 to 3.1)	
Week 18	1.1 (0.1 to 4.0)	
Week 20	1.7 (0.3 to 4.8)	
Week 24	1.7 (0.3 to 4.8)	1.1 (0.1 to 3.9)
Week 28	1.7 (0.3 to 4.8)	
Week 32	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 36	3.4 (1.2 to 7.2)	
Week 40	2.8 (0.9 to 6.4)	
Week 44	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 48	2.2 (0.6 to 5.6)	0.6 (0.0 to 3.0)
Week 52	2.2 (0.6 to 5.6)	2.2 (0.6 to 5.6)
Week 56	2.2 (0.6 to 5.6)	1.1 (0.1 to 3.9)

Week 60	1.7 (0.3 to 4.8)	1.7 (0.3 to 4.8)
Week 64	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 68	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 72	2.2 (0.6 to 5.6)	1.7 (0.3 to 4.8)
Week 76	2.2 (0.6 to 5.6)	0.6 (0.0 to 3.0)
Week 80	1.7 (0.3 to 4.8)	1.7 (0.3 to 4.8)
Week 84	2.2 (0.6 to 5.6)	4.4 (1.9 to 8.5)
Week 88	2.8 (0.9 to 6.4)	3.9 (1.6 to 7.8)
Week 92	2.8 (0.9 to 6.3)	2.8 (0.9 to 6.3)
Week 96	2.2 (0.6 to 5.6)	3.9 (1.6 to 7.8)
Week 100	2.2 (0.6 to 5.6)	6.1 (3.1 to 10.6)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Loss of >= 10 letters in BCVA at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-0.2	

95 % Confidence Interval 2-Sided	-3.2 to 2.4

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Loss of >= 10 letters in BCVA at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-4.1	
95 % Confidence Interval 2-Sided	-8.4 to -0.1	

Percentage of participants who lost >= 15 ETDRS letters in Best Corrected Visual Acuity (BCVA) from Baseline at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants who lost >= 15 ETDRS letters in Best Corrected Visual Acuity (BCVA) from Baseline at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4		0.6 (0.0 to 3.0)
Week 6	1.1 (0.1 to 4.0)	
Week 8	0.6 (0.0 to 3.1)	

Week 12		0.6 (0.0 to 3.0)
Week 16	0.6 (0.0 to 3.1)	
Week 18	1.1 (0.1 to 4.0)	
Week 20	1.7 (0.3 to 4.8)	
Week 24	1.1 (0.1 to 4.0)	0.6 (0.0 to 3.0)
Week 28	1.7 (0.3 to 4.8)	
Week 32	1.7 (0.3 to 4.8)	
Week 36	2.8 (0.9 to 6.4)	
Week 40	2.2 (0.6 to 5.6)	
Week 44	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 48	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 52	1.1 (0.1 to 4.0)	1.7 (0.3 to 4.8)
Week 56	1.7 (0.3 to 4.8)	1.1 (0.1 to 3.9)
Week 60	1.7 (0.3 to 4.8)	1.7 (0.3 to 4.8)
Week 64	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 68	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)

Week 72	2.2 (0.6 to 5.6)	1.1 (0.1 to 3.9)
Week 76	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 80	1.7 (0.3 to 4.8)	0.6 (0.0 to 3.0)
Week 84	1.7 (0.3 to 4.8)	2.2 (0.6 to 5.6)
Week 88	1.7 (0.3 to 4.8)	2.2 (0.6 to 5.6)
Week 92	2.2 (0.6 to 5.6)	2.2 (0.6 to 5.6)
Week 96	2.2 (0.6 to 5.6)	2.2 (0.6 to 5.6)
Week 100	2.2 (0.6 to 5.6)	3.3 (1.2 to 7.1)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Loss of >= 15 letters in BCVA at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-0.7	
95 % Confidence Interval 2-Sided	-3.2 to 1.6	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Loss of >= 15 letters in BCVA at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference

Other Clopper-Pearson exact method	-1.3
95 % Confidence Interval 2-Sided	-4.8 to 2.0

Percentage of participants with an Absolute Best Corrected Visual Acuity (BCVA) >= 73 ETDRS letters at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants with an Absolute Best Corrected Visual Acuity (BCVA) >= 73 ETDRS letters at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	55.3 (47.7 to 62.7)	42.5 (35.2 to 50.1)
Week 6	64.8 (57.3 to 71.8)	49.7 (42.2 to 57.2)
Week 8	66.5 (59.1 to 73.3)	50.8 (43.3 to 58.3)
Week 12	66.5 (59.1 to 73.3)	59.7 (52.1 to 66.9)
Week 16	69.8 (62.5 to 76.5)	60.8 (53.3 to 67.9)
Week 18	71.5 (64.3 to 78.0)	64.6 (57.2 to 71.6)
Week 20	71.5 (64.3 to 78.0)	61.3 (53.8 to 68.5)

Week 24	73.2 (66.1 to 79.5)	60.2 (52.7 to 67.4)
Week 28	72.6 (65.5 to 79.0)	61.9 (54.4 to 69.0)
Week 32	73.7 (66.7 to 80.0)	59.1 (51.6 to 66.4)
Week 36	70.4 (63.1 to 77.0)	65.2 (57.8 to 72.1)
Week 40	69.8 (62.5 to 76.5)	60.2 (52.7 to 67.4)
Week 44	73.7 (66.7 to 80.0)	63.5 (56.1 to 70.5)
Week 48	70.9 (63.7 to 77.5)	61.3 (53.8 to 68.5)
Week 52	73.7 (66.7 to 80.0)	64.6 (57.2 to 71.6)
Week 56	72.6 (65.5 to 79.0)	66.9 (59.5 to 73.7)
Week 60	70.9 (63.7 to 77.5)	66.9 (59.5 to 73.7)
Week 64	74.3 (67.2 to 80.5)	68.5 (61.2 to 75.2)
Week 68	71.5 (64.3 to 78.0)	66.3 (58.9 to 73.1)
Week 72	73.7 (66.7 to 80.0)	65.2 (57.8 to 72.1)
Week 76	72.6 (65.5 to 79.0)	66.9 (59.5 to 73.7)
Week 80	70.9 (63.7 to 77.5)	64.1 (56.6 to 71.1)
Week 84	70.9 (63.7 to 77.5)	65.2 (57.8 to 72.1)

Week 88	72.6 (65.5 to 79.0)	63.5 (56.1 to 70.5)
Week 92	71.5 (64.3 to 78.0)	63.5 (56.1 to 70.5)
Week 96	70.4 (63.1 to 77.0)	62.4 (54.9 to 69.5)
Week 100	70.9 (63.7 to 77.5)	62.4 (54.9 to 69.5)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Absolute BCVA >= 73 letters at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	3.5	
95 % Confidence Interval 2-Sided	-4.9 to 12.0	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Absolute BCVA >= 73 letters at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	3.6	
95 % Confidence Interval 2-Sided	-5.4 to 12.6	

Mean change from Baseline in Central Subfield Thickness (CSFT) at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Mean change from Baseline in Central Subfield Thickness (CSFT) at each post-baseline visit for the study eye (units: Micrometers) Mean ± Standard Deviation		
Week 4	-128.2 ± 131.47	-113.9 ± 123.20
Week 6	-136.9 ± 135.57	-126.0 ± 124.82
Week 8	-155.4 ± 139.09	-130.8 ± 124.71
Week 12	-160.8 ± 137.23	-137.9 ± 132.30
Week 16	-179.1 ± 137.26	-145.3 ± 132.63
Week 18	-175.8 ± 139.10	-149.0 ± 132.28
Week 20	-183.7 ± 139.76	-151.0 ± 130.98
Week 24	-183.3 ± 143.14	-134.0 ± 136.67
Week 28	-192.0 ± 145.85	-161.4 ± 131.27
Week 32	-178.6 ± 138.5	-144.9 ± 135.93
Week 36	-163.5 ± 144.34	-162.9 ± 135.19
Week 40	-183.3 ± 139.84	-149.9 ± 132.66
Week 44	-193.3 ± 144.12	-163.5 ± 133.01
Week 48	-172.8 ± 141.83	-154.6 ± 130.54
Week 52	-196.5 ± 144.44	-165.0 ± 134.77
Week 56	-191.08 ± 148.02	-162.4 ± 132.53
Week 60	-189.8 ± 147.93	-166.2 ± 132.61
Week 64	-193.2 ± 143.36	-160.2 ± 137.83
Week 68	-194.5 ± 141.47	-169.8 ± 143.97

Week 72	-190.4 ± 142.25	-165.1 ± 141.38
Week 76	-185.6 ± 143.68	-174.7 ± 138.70
Week 80	-185.7 ± 145.52	-171.1 ± 138.53
Week 84	-193.5 ± 142.53	-175.1 ± 139.76
Week 88	-191.0 ± 141.29	-172.2 ± 138.08
Week 92	-193.8 ± 142.07	-180.1 ± 138.88
Week 96	-197.2 ± 144.29	-170.2 ± 154.37
Week 100	-201.4 ± 142.90	-173.9 ± 152.03

Average mean change from Baseline in Central Subfield Thickness (CSFT) over the period Week 40 through Week 52 / Week 88 through Week 100 for the study eye

(Time Frame: Baseline, period Week 40 through Week 52, period Week 88 through Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Average mean change from Baseline in Central Subfield Thickness (CSFT) over the period Week 40 through Week 52 / Week 88 through Week 100 for the study eye (units: Micrometers) Least Squares Mean (95% Confidence Interval)		
period Week 40 through Week 52	-187.1 (-200.7 to -173.5)	-157.7 (-171.2 to -144.1)
period Week 88 through Week 100	-196.6 (-210.9 to -182.3)	-173.4 (-187.6 to -159.1)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	CSFT over period Week 40 through Week 52

Non-Inferiority/Equivalence Test	Other	Treatment difference
P Value	<0.003	
Method	ANOVA	
Other LS mean difference	-29.4	
Standard Error of the mean	9.76	
95 % Confidence Interval 2-Sided	-48.6 to -10.2	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	CSFT over period Week 40 through Week 52
P Value	0.001	
Method	ANOVA	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	CSFT over period Week 88 through Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	-23.2	
Standard Error of the mean	10.28	
95 % Confidence Interval 2-Sided	-43.5 to -3.0	

Average mean change from baseline in CSFT over the period Week 4 to Week 52 / 100 for the study eye

(Time Frame: Baseline, period Week 4 through Week 52, period Week 4 through Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Average mean change from baseline in CSFT over the period Week 4 to Week 52 / 100 for the study eye (units: Micrometers) Least Squares Mean (95% Confidence Interval)		
period Week 4 through Week 52	-172.8 (-185.8 to -159.8)	-145.4 (-158.4 to -132.4)
period Week 4 through Week 100	-181.8 (-194.7 to -168.9)	-156.1 (-169.0 to -143.2)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	CSFT over period Week 4 through Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	-27.4	
Standard Error of the mean	9.35	
95 % Confidence Interval 2-Sided	-45.8 to -9.0	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	CSFT over period Week 4 through Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other LS mean difference	-25.8	

Standard Error of the mean	9.29
95 % Confidence Interval 2-Sided	-44.0 to -7.5

Percentage of participants with normal CSFT thickness (<280 micrometers) at each post-baseline visit for the study eye

(Time Frame: Baseline, Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants with normal CSFT thickness (<280 micrometers) at each post-baseline visit for the study eye (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	12.8 (8.3 to 18.7)	13.3 (8.7 to 19.2)
Week 6	16.8 (11.6 to 23.1)	14.4 (9.7 to 20.4)
Week 8	22.9 (17.0 to 29.8)	16.7 (11.5 to 22.9)
Week 12	30.2 (23.5 to 37.5)	24.4 (18.4 to 31.4)
Week 16	36.9 (29.8 to 44.4)	29.4 (22.9 to 36.7)
Week 18	39.1 (31.9 to 46.7)	30.0 (23.4 to 37.3)
Week 20	42.5 (35.1 to 50.1)	31.1 (24.4 to 38.4)

Week 24	48.6 (41.1 to 56.2)	29.4 (22.9 to 36.7)
Week 28	50.3 (42.7 to 57.8)	33.9 (27.0 to 41.3)
Week 32	48.0 (40.5 to 55.6)	30.6 (23.9 to 37.8)
Week 36	38.5 (31.4 to 46.1)	38.9 (31.7 to 46.4)
Week 40	51.4 (43.8 to 58.9)	37.2 (30.1 to 44.7)
Week 44	51.4 (43.8 to 58.9)	38.9 (31.7 to 46.4)
Week 48	49.7 (42.2 to 57.3)	37.2 (30.1 to 44.7)
Week 52	57.5 (49.9 to 64.9)	41.4 (34.2 to 49.0)
Week 56	57.5 (49.9 to 64.9)	40.3 (33.1 to 47.9)
Week 60	53.1 (45.5 to 60.6)	40.3 (33.1 to 47.9)
Week 64	54.2 (46.6 to 61.6)	38.1 (31.0 to 45.6)
Week 68	53.6 (46.0 to 61.1)	41.4 (34.2 to 49.0)
Week 72	56.4 (48.8 to 63.8)	38.7 (31.5 to 46.2)
Week 76	55.3 (47.7 to 62.7)	42.5 (35.2 to 50.1)
Week 80	57.0 (49.4 to 64.3)	39.8 (32.6 to 47.3)
Week 84	57.0 (49.4 to 64.3)	43.1 (35.8 to 50.6)

Week 88	56.4 (48.8 to 63.8)	41.4 (34.2 to 49.0)
Week 92	57.0 (49.4 to 64.3)	45.9 (38.4 to 53.4)
Week 96	59.8 (52.2 to 67.0)	43.6 (36.3 to 51.2)
Week 100	62.0 (54.5 to 69.1)	47.0 (39.5 to 54.5)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	CSFT thickness (<280 micrometers) at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	16.3	
95 % Confidence Interval 2-Sided	5.7 to 25.9	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	CSFT thickness (<280 micrometers) at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	14.7	
95 % Confidence Interval 2-Sided	4.2 to 24.9	

Percentage of patients with presence of Subretinal Fluid (SRF) in the study eye at each post-baseline visit

(Time Frame: Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of patients with presence of Subretinal Fluid (SRF) in the study eye at each post-baseline visit (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	12.3 (7.9 to 18.0)	19.3 (13.9 to 25.9)
Week 6	10.1 (6.1 to 15.4)	13.8 (9.1 to 19.7)
Week 8	5.6 (2.7 to 10.0)	12.2 (7.8 to 17.8)
Week 12	3.9 (1.6 to 7.9)	7.7 (4.3 to 12.6)
Week 16	1.7 (0.3 to 4.8)	3.9 (1.6 to 7.8)
Week 18	2.2 (0.6 to 5.6)	2.2 (0.6 to 5.6)
Week 20	1.7 (0.3 to 4.8)	3.3 (1.2 to 7.1)
Week 24	2.2 (0.6 to 5.6)	6.6 (3.5 to 11.3)
Week 28	2.2 (0.6 to 5.6)	2.8 (0.9 to 6.3)
Week 32	5.0 (2.3 to 9.3)	3.9 (1.6 to 7.8)
Week 36	6.7 (3.5 to 11.4)	1.7 (0.3 to 4.8)

Week 40	4.5 (1.9 to 8.6)	2.8 (0.9 to 6.3)
Week 44	2.2 (0.6 to 5.6)	2.8 (0.9 to 6.3)
Week 48	6.1 (3.1 to 10.7)	5.0 (2.3 to 9.2)
Week 52	1.7 (0.3 to 4.8)	3.3 (1.2 to 7.1)
Week 56	2.8 (0.9 to 6.4)	2.2 (0.6 to 5.6)
Week 60	2.8 (0.9 to 6.4)	2.2 (0.6 to 5.6)
Week 64	2.2 (0.6 to 5.6)	3.9 (1.6 to 7.8)
Week 68	3.4 (1.2 to 7.2)	4.4 (1.9 to 8.5)
Week 72	3.4 (1.2 to 7.2)	2.8 (0.9 to 6.3)
Week 76	3.9 (1.6 to 7.9)	2.2 (0.6 to 5.6)
Week 80	4.5 (1.9 to 8.6)	2.2 (0.6 to 5.6)
Week 84	2.2 (0.6 to 5.6)	2.2 (0.6 to 5.6)
Week 88	3.4 (1.2 to 7.2)	2.2 (0.6 to 5.6)
Week 92	1.7 (0.3 to 4.8)	1.1 (0.1 to 3.9)
Week 96	2.2 (0.6 to 5.6)	2.8 (0.9 to 6.3)
Week 100	2.2 (0.6 to 5.6)	2.8 (0.9 to 6.3)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Subretinal Fluid (SRF) at Week 52
Other Clopper-Pearson exact method	-1.2	
95 % Confidence Interval 2-Sided	-4.5 to 2.1	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Subretinal Fluid (SRF) at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment Difference
Other Clopper-Pearson exact method	-0.2	
95 % Confidence Interval 2-Sided	-3.4 to 3.4	

Percentage of patients with presence of Intraretinal Fluid (IRF) in the study eye at each post-baseline visit

(Time Frame: Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181

Percentage of patients with presence of Intraretinal Fluid (IRF) in the study eye at each post-baseline visit
(units: Percentage of Participants)
Number (95% Confidence Interval)

Week 4	88.3 (82.6 to 92.6)	89.0 (83.5 to 93.1)
Week 6	85.5 (79.4 to 90.3)	86.2 (80.3 to 90.9)
Week 8	87.2 (81.3 to 91.7)	84.5 (78.4 to 89.5)
Week 12	83.8 (77.6 to 88.9)	85.6 (79.7 to 90.4)
Week 16	76.0 (69.0 to 82.0)	84.0 (77.8 to 89.0)
Week 18	77.7 (70.8 to 83.5)	81.2 (74.8 to 86.6)
Week 20	72.6 (65.5 to 79.0)	79.6 (72.9 to 85.2)
Week 24	69.8 (62.5 to 76.5)	82.3 (76.0 to 87.6)
Week 28	67.6 (60.2 to 74.4)	75.1 (68.2 to 81.3)
Week 32	67.6 (60.2 to 74.4)	76.8 (70.0 to 82.7)
Week 36	73.2 (66.1 to 79.5)	72.4 (65.3 to 78.7)
Week 40	57.5 (49.9 to 64.9)	74.0 (67.0 to 80.3)
Week 44	56.4 (48.8 to 63.8)	71.3 (64.1 to 77.7)
Week 48	60.9 (53.3 to 68.1)	75.7 (68.8 to 81.7)
Week 52	53.6 (46.0 to 61.1)	72.9 (65.8 to 79.3)
Week 56	51.4 (43.8 to 58.9)	70.2 (62.9 to 76.7)

Week 60	55.3 (47.7 to 62.7)	69.1 (61.8 to 75.7)
Week 64	48.6 (41.1 to 56.2)	69.6 (62.4 to 76.2)
Week 68	47.5 (40.0 to 55.1)	66.9 (59.5 to 73.7)
Week 72	45.8 (38.4 to 53.4)	66.9 (59.5 to 73.7)
Week 76	50.3 (42.7 to 57.8)	63.0 (55.5 to 70.0)
Week 80	45.8 (38.4 to 53.4)	65.7 (58.3 to 72.6)
Week 84	40.2 (33.0 to 47.8)	63.0 (55.5 to 70.0)
Week 88	48.0 (40.5 to 55.6)	64.1 (56.6 to 71.1)
Week 92	44.7 (37.3 to 52.3)	59.1 (51.6 to 66.4)
Week 96	41.3 (34.0 to 48.9)	61.9 (54.4 to 69.0)
Week 100	40.8 (33.5 to 48.4)	56.9 (49.4 to 64.2)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Intraretinal Fluid (IRF) at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment Difference
Other Clopper-Pearson exact method	-19.1	

95 % Confidence Interval 2-Sided	-28.9 to -9.2

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Intraretinal Fluid (IRF) at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment Difference
Other Clopper-Pearson exact method	-16.1	
95 % Confidence Interval 2-Sided	-26.3 to -5.7	

Percentage of patients with presence of Subretinal Fluid (SRF) and/or Intraretinal Fluid (IRF) in the study eye at each post-baseline visit

(Time Frame: Week 4, Week 6, Week 8, Week 12, Week 16, Week 18, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of patients with presence of Subretinal Fluid (SRF) and/or Intraretinal Fluid (IRF) in the study eye at each post-baseline visit (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 4	90.5 (85.2 to 94.4)	90.6 (85.4 to 94.4)
Week 6	86.6 (80.7 to 91.2)	88.4 (82.8 to 92.7)
Week 8	87.2 (81.3 to 91.7)	85.6 (79.7 to 90.4)

Week 12	83.8 (77.6 to 88.9)	86.2 (80.3 to 90.9)
Week 16	76.0 (69.0 to 82.0)	84.0 (77.8 to 89.0)
Week 18	78.2 (71.4 to 84.0)	81.2 (74.8 to 86.6)
Week 20	73.2 (66.1 to 79.5)	79.6 (72.9 to 85.2)
Week 24	70.4 (63.1 to 77.0)	82.3 (76.0 to 87.6)
Week 28	68.7 (61.4 to 75.4)	75.1 (68.2 to 81.3)
Week 32	68.7 (61.4 to 75.4)	76.8 (70.0 to 82.7)
Week 36	73.7 (66.7 to 80.0)	72.4 (65.3 to 78.7)
Week 40	58.1 (50.5 to 65.4)	74.0 (67.0 to 80.3)
Week 44	57.0 (49.4 to 64.3)	71.3 (64.1 to 77.7)
Week 48	61.5 (53.9 to 68.6)	75.7 (68.8 to 81.7)
Week 52	54.2 (46.6 to 61.6)	72.9 (65.8 to 79.3)
Week 56	52.0 (44.4 to 59.5)	70.2 (62.9 to 76.7)
Week 60	55.3 (47.7 to 62.7)	69.1 (61.8 to 75.7)
Week 64	49.2 (41.6 to 56.7)	69.6 (62.4 to 76.2)
Week 68	48.0 (40.5 to 55.6)	68.0 (60.6 to 74.7)

Week 72	46.9 (39.4 to 54.5)	66.9 (59.5 to 73.7)
Week 76	50.8 (43.3 to 58.4)	63.0 (55.5 to 70.0)
Week 80	46.4 (38.9 to 54.0)	65.7 (58.3 to 72.6)
Week 84	40.8 (33.5 to 48.4)	63.0 (55.5 to 70.0)
Week 88	48.6 (41.1 to 56.2)	64.1 (56.6 to 71.1)
Week 92	45.3 (37.8 to 52.8)	59.1 (51.6 to 66.4)
Week 96	41.3 (34.0 to 48.9)	61.9 (54.4 to 69.0)
Week 100	40.8 (33.5 to 48.4)	56.9 (49.4 to 64.2)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Subretinal Fluid (SRF) and/or Intraretinal Fluid (IRF) at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment Difference
Other Clopper-Pearson exact method	-18.4	
95 % Confidence Interval 2-Sided	-28.5 to -8.3	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Subretinal Fluid (SRF) and/or Intraretinal Fluid (IRF) at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference

Other Clopper-Pearson exact method	-16.2
95 % Confidence Interval 2-Sided	-26.4 to -5.9

Percentage of participants with presence of leakage on Fluorescein Angiography (FA) at Weeks 52 and 100

(Time Frame: Week 52, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants with presence of leakage on Fluorescein Angiography (FA) at Weeks 52 and 100 (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 52	54.7 (47.2 to 62.2)	79.4 (72.8 to 85.1)
Week 100	46.9 (39.4 to 54.5)	65.6 (58.1 to 72.5)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Fluorescein Angiography (FA) at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-25.4	
95 % Confidence Interval 2-Sided	-34.4 to -16.3	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Fluorescein Angiography (FA) at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-19.1	
95 % Confidence Interval 2-Sided	-29.1 to -8.2	

Percentage of Participants with with >=2-step improvement from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of Participants with with >=2-step improvement from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 28	25.0 (18.8 to 32.1)	20.9 (15.2 to 27.6)
Week 52	29.0 (22.4 to 36.3)	27.7 (21.2 to 34.9)
Week 76	30.1 (23.4 to 37.5)	30.5 (23.8 to 37.9)
Week 100	35.8 (28.7 to 43.4)	31.1 (24.3 to 38.5)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=2-step improvement in ETDRS-DRSS at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	1.1	
95 % Confidence Interval 2-Sided	-5.6 to 7.8	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=2-step improvement in ETDRS-DRSS at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	4.5	
95 % Confidence Interval 2-Sided	-1.7 to 10.8	

Percentage of Participants with with >=3-step improvement from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of Participants with with >=3-step improvement from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 28	13.1 (8.5 to 19.0)	11.3 (7.0 to 16.9)

Week 52	14.8 (9.9 to 20.9)	15.3 (10.3 to 21.4)
Week 76	18.8 (13.3 to 25.3)	15.3 (10.3 to 21.4)
Week 100	21.0 (15.3 to 27.8)	16.9 (11.7 to 23.3)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=3-step improvement in ETDRS-DRSS at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-0.6	
95 % Confidence Interval 2-Sided	-7.1 to 5.7	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=3-step improvement in ETDRS-DRSS at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	3.9	
95 % Confidence Interval 2-Sided	-2.3 to 10.0	

Percentage of Participants with with >=2-step worsening from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**

Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of Participants with with >=2-step worsening from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 28	2.3 (0.6 to 5.7)	0.6 (0.0 to 3.1)
Week 52	1.7 (0.4 to 4.9)	0.6 (0.0 to 3.1)
Week 76	3.4 (1.3 to 7.3)	0.6 (0.0 to 3.1)
Week 100	4.5 (2.0 to 8.8)	1.7 (0.4 to 4.9)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=2-step worsening in ETDRS-DRSS at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	1.1	
95 % Confidence Interval 2-Sided	-1.0 to 3.6	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=2-step worsening in ETDRS-DRSS at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference

Other Clopper-Pearson exact method	2.9
95 % Confidence Interval 2-Sided	-0.5 to 6.9

Percentage of Participants with with >=3-step worsening from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of Participants with with >=3-step worsening from Baseline in ETDRS Diabetic Retinopathy Severity Scale (ETDRS-DRSS) score (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 28	0.6 (0.0 to 3.1)	
Week 52	0.6 (0.0 to 3.1)	
Week 76	0.6 (0.0 to 3.1)	
Week 100	0.6 (0.0 to 3.1)	1.1 (0.1 to 4.0)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=3-step worsening in ETDRS-DRSS at Week 52
Non-Inferiority/Equivalence Test	Other	Treatment difference

Other Clopper-Pearson exact method	0.6
95 % Confidence Interval 2-Sided	0.5 to 2.1

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	>=3-step worsening in ETDRS-DRSS at Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-0.6	
95 % Confidence Interval 2-Sided	-2.6 to 1.3	

Percentage of participants with progression to proliferative diabetic retinopathy (PDR) as assessed by ETDRS-DRSS Score of at least 61 by Week 100

(Time Frame: Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Percentage of participants with progression to proliferative diabetic retinopathy (PDR) as assessed by ETDRS-DRSS Score of at least 61 by Week 100 (units: Percentage of Participants) Number (95% Confidence Interval)		
Week 100	0.6 (0.0 to 3.4)	0.6 (0.0 to 3.4)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	Proliferative diabetic retinopathy (PDR) of at least 61 by Week 100
Non-Inferiority/Equivalence Test	Other	Treatment difference
Other Clopper-Pearson exact method	-0.0	
95 % Confidence Interval 2-Sided	-2.1 to 1.9	

Number of Participants with Ocular and Non-ocular Adverse Events (AEs)

(Time Frame: From randomization till 30 days safety follow-up, assessed up to 35 months.)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Number of Participants with Ocular and Non-ocular Adverse Events (AEs) (units: Participants) Count of Participants (Not Applicable)		
Ocular adverse events : Mild	52 (71.23%)	47 (63.51%)
Ocular adverse events : Moderate	15 (20.55%)	23 (31.08%)
Ocular adverse events : Severe	6 (8.22%)	4 (5.41%)
Non-ocular adverse events : Mild	52 (38.24%)	51 (36.17%)
Non-ocular adverse events : Moderate	51 (37.5%)	50 (35.46%)

Non-ocular adverse events : Severe	33 (24.26%)	40 (28.37%)

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): composite score

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): composite score (units: Score on a scale) Mean ± Standard Deviation		
Week 28	5.7 ± 11.91	6.3 ± 10.19
Week 52	8.9 ± 11.67	6.7 ± 12.12
Week 76	9.8 ± 12.22	7.6 ± 11.81
Week 100	9.0 ± 12.94	6.2 ± 14.13

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - General Vision

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - General Vision (units: Score on a scale) Mean ± Standard Deviation		

Week 28	9.0 ± 16.11	10.2 ± 15.63
Week 52	11.2 ± 17.05	10.5 ± 17.14
Week 76	12.4 ± 16.49	12.0 ± 16.40
Week 100	12.0 ± 16.25	10.1 ± 18.73

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Ocular Pain

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Ocular Pain (units: Score on a scale) Mean ± Standard Deviation		
Week 28	4.1 ± 19.52	4.6 ± 18.48
Week 52	4.6 ± 18.75	4.4 ± 17.92
Week 76	6.2 ± 16.95	4.6 ± 18.68
Week 100	4.3 ± 16.60	5.4 ± 20.77

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Near Activities

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks

Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Near Activities (units: Score on a scale) Mean ± Standard Deviation		
Week 28	6.4 ± 20.83	6.3 ± 18.42
Week 52	10.5 ± 20.30	9.3 ± 19.57
Week 76	11.0 ± 21.91	9.2 ± 18.76
Week 100	13.0 ± 20.21	7.3 ± 21.71

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Distance Activities

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Distance Activities (units: Score on a scale) Mean ± Standard Deviation		
Week 28	6.2 ± 18.87	5.6 ± 15.78
Week 52	11.7 ± 17.62	8.2 ± 17.12
Week 76	12.1 ± 18.32	8.1 ± 16.71
Week 100	11.4 ± 18.94	6.6 ± 19.07

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Social Functioning

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Social Functioning (units: Score on a scale) Mean ± Standard Deviation		
Week 28	3.3 ± 15.82	4.4 ± 16.48
Week 52	7.1 ± 16.22	4.9 ± 15.59
Week 76	6.3 ± 16.65	5.0 ± 15.34
Week 100	6.1 ± 16.78	4.1 ± 17.55

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Mental Health

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Mental Health (units: Score on a scale) Mean ± Standard Deviation		
Week 28	7.9 ± 19.53	10.1 ± 19.90
Week 52	12.6 ± 22.42	10.1 ± 22.78
Week 76	13.5 ± 21.02	13.1 ± 23.10
Week 100	13.3 ± 20.91	11.6 ± 26.31

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Role Difficulties

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Role Difficulties (units: Score on a scale) Mean ± Standard Deviation		
Week 28	6.9 ± 25.13	9.4 ± 23.41
Week 52	12.2 ± 24.76	8.7 ± 27.21
Week 76	14.0 ± 28.44	11.4 ± 27.83
Week 100	12.3 ± 28.14	10.2 ± 27.12

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Dependency

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Dependency (units: Score on a scale) Mean ± Standard Deviation		
Week 28	5.5 ± 19.39	3.6 ± 20.34

Week 52	7.6 ± 19.53	3.9 ± 22.49
Week 76	7.3 ± 20.19	5.6 ± 23.24
Week 100	6.8 ± 19.85	2.9 ± 24.79

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Driving

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Driving (units: Score on a scale) Mean ± Standard Deviation		
Week 28	1.4 ± 18.75	4.8 ± 12.24
Week 52	6.4 ± 14.63	4.2 ± 12.81
Week 76	8.9 ± 15.95	2.8 ± 15.88
Week 100	5.4 ± 15.81	1.2 ± 16.75

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Color Vision

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Color Vision (units: Score on a scale) Mean ± Standard Deviation		
Week 28	3.5 ± 15.10	4.2 ± 12.50
Week 52	5.8 ± 15.08	3.6 ± 13.09
Week 76	5.2 ± 15.73	3.9 ± 13.79
Week 100	4.3 ± 14.70	3.2 ± 15.48

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Peripheral Vision

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): subscale score - Peripheral Vision (units: Score on a scale) Mean ± Standard Deviation		
Week 28	5.3 ± 18.83	4.0 ± 16.99
Week 52	7.2 ± 18.68	3.2 ± 19.77
Week 76	9.3 ± 19.64	4.3 ± 17.82
Week 100	8.5 ± 19.33	2.3 ± 19.37

Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): General Health Rating

(Time Frame: Baseline, Week 28, Week 52, Week 76, Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg

Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	181
Change from Baseline in the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25): General Health Rating (units: Score on a scale) Mean ± Standard Deviation		
Week 28	3.9 ± 18.66	4.3 ± 19.92
Week 52	5.8 ± 22.34	4.8 ± 23.12
Week 76	8.9 ± 21.21	7.1 ± 22.57
Week 100	6.7 ± 19.14	5.7 ± 21.80

Systemic brolucizumab concentration

(Time Frame: Up to Week 24)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	0
Systemic brolucizumab concentration (units: ng/mL) Mean ± Standard Deviation		
Day 2	56.2 ± 10.4	
Week 4	0.760 ± 1.98	
Week 12	NA ± NA[12]	
Week 24	NA ± NA[12]	
Week 24 + 1 Day	41.5 ± 80.5	

[1] NA = not estimable: Below the limit of quantitation (<0.5 ng/mL)
[2] NA = not estimable: Below the limit of quantitation (<0.5 ng/mL)

Distribution of integrated Anti-Drug Antibody (ADA) status in the brolucizumab arm

(Time Frame: Up to Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	0
Distribution of integrated Anti-Drug Antibody (ADA) status in the brolucizumab arm (units: Participants) Count of Participants (Not Applicable)		
ADA negative or ADA positive with no boost	146 (81.56%)	(NaN%)
Induced or Boosted	27 (15.08%)	(NaN%)
Missing ADA at pre-dose or no post-dose ADA data	6 (3.35%)	(NaN%)

Distribution of integrated Anti-Drug Antibody (ADA) status in the brolucizumab arm - adjusted for pre-existing ADA status

(Time Frame: Up to Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	0
Distribution of integrated Anti-Drug Antibody (ADA) status in the brolucizumab arm - adjusted for pre-existing ADA status (units: Participants) Count of Participants (Not Applicable)		

ADA negative/ADA Negative or titer value of 40 at pre-dose	53 (63.1%)	(NaN%)
ADA positive with no boost/ADA Positive at pre-dose	93 (84.55%)	(NaN%)
Induced/ADA Negative at pre-dose	14 (21.88%)	(NaN%)
Boosted/ADA Positive at pre-dose	13 (11.82%)	(NaN%)

Pre-existing ADA status and incidence of Adverse Event of Special Interest (AESI) in the study eye

(Time Frame: Up to Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	0
Pre-existing ADA status and incidence of Adverse Event of Special Interest (AESI) in the study eye (units: Participants) Count of Participants (Not Applicable)		
Negative : At least 1 AESI	1 (1.56%)	(NaN%)
Negative : No AESI	63 (98.44%)	(NaN%)
Postive : At least 1 AESI	5 (4.55%)	(NaN%)
Postive : No AESI	105 (95.45%)	(NaN%)

Integrated ADA status up to Week 100 and incidence of Adverse Event of Special Interest (AESI) in the study eye.

(Time Frame: Up to Week 100)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks
Number of Participants Analyzed [units: participants]	179	0
Integrated ADA status up to Week 100 and incidence of Adverse Event of Special Interest (AESI) in the study eye. (units: Participants) Count of Participants (Not Applicable)		
ADA-negative or no boost : At least 1 AESI	4 (2.74%)	(NaN%)
ADA-negative or no boost : No AESI	142 (97.26%)	(NaN%)
Induced or boosted : At least 1 AESI	2 (7.41%)	(NaN%)
Induced or boosted : No AESI	25 (92.59%)	(NaN%)

Safety Results

All-Cause Mortality

	Brolucizumab 6mg N = 179	Aflibercept 2mg N = 181	Overall N = 360
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks	Overall
Total participants affected	13 (7.26%)	9 (4.97%)	22 (6.11%)

Serious Adverse Events by System Organ Class

Time Frame	From first dose of study treatment up to 30 days after last dose (maximum 35 months)
Additional Description	Adverse Events (AEs) and All-cause mortality were collected in the Safety Set
Source Vocabulary for Table Default	MedDRA (24.0)
Assessment Type for Table Default	Systematic Assessment

	Brolucizumab 6mg N = 179	Aflibercept 2mg N = 181	Overall N = 360
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks	Overall
Total participants affected	53 (29.61%)	60 (33.15%)	113 (31.39%)
Blood and lymphatic system disorders			
Anaemia	1 (0.56%)	1 (0.55%)	2 (0.56%)
Iron deficiency anaemia	0 (0.00%)	2 (1.10%)	2 (0.56%)
Microcytic anaemia	0 (0.00%)	1 (0.55%)	1 (0.28%)

Cardiac disorders			
Acute coronary syndrome	0 (0.00%)	1 (0.55%)	1 (0.28%)
Acute myocardial infarction	0 (0.00%)	2 (1.10%)	2 (0.56%)
Angina pectoris	2 (1.12%)	0 (0.00%)	2 (0.56%)
Aortic valve stenosis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Atrial fibrillation	0 (0.00%)	1 (0.55%)	1 (0.28%)
Atrial flutter	1 (0.56%)	0 (0.00%)	1 (0.28%)
Cardiac arrest	0 (0.00%)	2 (1.10%)	2 (0.56%)
Cardiac failure	2 (1.12%)	4 (2.21%)	6 (1.67%)
Cardiac failure acute	1 (0.56%)	1 (0.55%)	2 (0.56%)
Cardiac failure congestive	1 (0.56%)	0 (0.00%)	1 (0.28%)
Cardiogenic shock	1 (0.56%)	0 (0.00%)	1 (0.28%)
Cardiopulmonary failure	1 (0.56%)	1 (0.55%)	2 (0.56%)
Coronary artery disease	1 (0.56%)	2 (1.10%)	3 (0.83%)
Coronary artery stenosis	2 (1.12%)	1 (0.55%)	3 (0.83%)
Myocardial infarction	0 (0.00%)	3 (1.66%)	3 (0.83%)
Myocardial ischaemia	1 (0.56%)	0 (0.00%)	1 (0.28%)
Ear and labyrinth disorders			
Vertigo positional	0 (0.00%)	1 (0.55%)	1 (0.28%)
Endocrine disorders			
Goitre	0 (0.00%)	1 (0.55%)	1 (0.28%)
Eye disorders			
Glaucoma - Study eye	1 (0.56%)	0 (0.00%)	1 (0.28%)
Retinal artery occlusion - Study eye	1 (0.56%)	0 (0.00%)	1 (0.28%)

Retinal detachment - Study eye	0 (0.00%)	1 (0.55%)	1 (0.28%)
Retinal tear - Study eye	0 (0.00%)	1 (0.55%)	1 (0.28%)
Uveitis - Fellow eye	0 (0.00%)	1 (0.55%)	1 (0.28%)
Uveitis - Study eye	1 (0.56%)	1 (0.55%)	2 (0.56%)
Vitreous haemorrhage - Fellow eye	1 (0.56%)	1 (0.55%)	2 (0.56%)
Gastrointestinal disorders			
Abdominal pain upper	0 (0.00%)	1 (0.55%)	1 (0.28%)
Diarrhoea	0 (0.00%)	2 (1.10%)	2 (0.56%)
Duodenal ulcer	0 (0.00%)	1 (0.55%)	1 (0.28%)
Dyspepsia	0 (0.00%)	1 (0.55%)	1 (0.28%)
Inguinal hernia	1 (0.56%)	1 (0.55%)	2 (0.56%)
Pancreatitis acute	0 (0.00%)	1 (0.55%)	1 (0.28%)
Rectal haemorrhage	2 (1.12%)	0 (0.00%)	2 (0.56%)
General disorders and administration site conditions			
Death	1 (0.56%)	2 (1.10%)	3 (0.83%)
Mass	1 (0.56%)	0 (0.00%)	1 (0.28%)
Oedema peripheral	1 (0.56%)	0 (0.00%)	1 (0.28%)
Sudden death	1 (0.56%)	0 (0.00%)	1 (0.28%)
Hepatobiliary disorders			
Cholecystitis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Cholecystitis chronic	1 (0.56%)	0 (0.00%)	1 (0.28%)
Cholelithiasis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Immune system disorders			

Anaphylactic reaction	1 (0.56%)	0 (0.00%)	1 (0.28%)
Infections and infestations			
Bone abscess	0 (0.00%)	1 (0.55%)	1 (0.28%)
Cellulitis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Clostridium difficile colitis	0 (0.00%)	1 (0.55%)	1 (0.28%)
COVID-19	4 (2.23%)	3 (1.66%)	7 (1.94%)
COVID-19 pneumonia	1 (0.56%)	0 (0.00%)	1 (0.28%)
Endophthalmitis - Study eye	2 (1.12%)	1 (0.55%)	3 (0.83%)
Erysipelas	1 (0.56%)	1 (0.55%)	2 (0.56%)
Fungal oesophagitis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Gangrene	3 (1.68%)	2 (1.10%)	5 (1.39%)
Gastroenteritis	0 (0.00%)	2 (1.10%)	2 (0.56%)
Herpes zoster	1 (0.56%)	0 (0.00%)	1 (0.28%)
Localised infection	0 (0.00%)	1 (0.55%)	1 (0.28%)
Ophthalmic herpes zoster - Study eye	1 (0.56%)	0 (0.00%)	1 (0.28%)
Orchitis	1 (0.56%)	0 (0.00%)	1 (0.28%)
Osteomyelitis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Pneumonia	4 (2.23%)	3 (1.66%)	7 (1.94%)
Pneumonia viral	1 (0.56%)	0 (0.00%)	1 (0.28%)
Pyelonephritis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Sepsis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Streptococcal infection	1 (0.56%)	0 (0.00%)	1 (0.28%)
Urinary tract infection	0 (0.00%)	2 (1.10%)	2 (0.56%)
Urosepsis	1 (0.56%)	0 (0.00%)	1 (0.28%)

Injury, poisoning and procedural complications			
Femoral neck fracture	0 (0.00%)	2 (1.10%)	2 (0.56%)
Fracture	0 (0.00%)	1 (0.55%)	1 (0.28%)
Joint dislocation	0 (0.00%)	1 (0.55%)	1 (0.28%)
Subdural haematoma	1 (0.56%)	0 (0.00%)	1 (0.28%)
Wrist fracture	0 (0.00%)	1 (0.55%)	1 (0.28%)
Investigations			
Haemoglobin decreased	1 (0.56%)	0 (0.00%)	1 (0.28%)
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control	1 (0.56%)	0 (0.00%)	1 (0.28%)
Fluid overload	1 (0.56%)	0 (0.00%)	1 (0.28%)
Fluid retention	0 (0.00%)	2 (1.10%)	2 (0.56%)
Gout	0 (0.00%)	1 (0.55%)	1 (0.28%)
Hypoglycaemia	1 (0.56%)	1 (0.55%)	2 (0.56%)
Type 1 diabetes mellitus	1 (0.56%)	0 (0.00%)	1 (0.28%)
Musculoskeletal and connective tissue disorders			
Arthralgia	1 (0.56%)	1 (0.55%)	2 (0.56%)
Intervertebral disc protrusion	1 (0.56%)	0 (0.00%)	1 (0.28%)
Osteonecrosis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign oesophageal neoplasm	1 (0.56%)	0 (0.00%)	1 (0.28%)
Biliary neoplasm	1 (0.56%)	0 (0.00%)	1 (0.28%)
Bronchial carcinoma	0 (0.00%)	1 (0.55%)	1 (0.28%)

Cholangiocarcinoma	0 (0.00%)	1 (0.55%)	1 (0.28%)
Colon adenoma	0 (0.00%)	1 (0.55%)	1 (0.28%)
Colon cancer stage I	1 (0.56%)	0 (0.00%)	1 (0.28%)
Gastric cancer	1 (0.56%)	1 (0.55%)	2 (0.56%)
Hepatic cancer	1 (0.56%)	0 (0.00%)	1 (0.28%)
Lung neoplasm malignant	0 (0.00%)	1 (0.55%)	1 (0.28%)
Malignant neoplasm of unknown primary site	0 (0.00%)	1 (0.55%)	1 (0.28%)
Metastasis	1 (0.56%)	0 (0.00%)	1 (0.28%)
Neoplasm malignant	0 (0.00%)	1 (0.55%)	1 (0.28%)
Ovarian cancer	1 (0.56%)	0 (0.00%)	1 (0.28%)
Pleomorphic adenoma	0 (0.00%)	1 (0.55%)	1 (0.28%)
Squamous cell carcinoma of lung	1 (0.56%)	0 (0.00%)	1 (0.28%)
Waldenstrom's macroglobulinaemia	0 (0.00%)	1 (0.55%)	1 (0.28%)
Nervous system disorders			
Arachnoiditis	0 (0.00%)	1 (0.55%)	1 (0.28%)
Bickerstaff's encephalitis	1 (0.56%)	0 (0.00%)	1 (0.28%)
Carotid artery stenosis	1 (0.56%)	0 (0.00%)	1 (0.28%)
Cerebellar haemorrhage	0 (0.00%)	1 (0.55%)	1 (0.28%)
Cerebellar stroke	1 (0.56%)	0 (0.00%)	1 (0.28%)
Cerebrovascular accident	2 (1.12%)	2 (1.10%)	4 (1.11%)
Haemorrhagic stroke	1 (0.56%)	0 (0.00%)	1 (0.28%)
Headache	0 (0.00%)	1 (0.55%)	1 (0.28%)
Hemiparesis	1 (0.56%)	0 (0.00%)	1 (0.28%)
Hypoglycaemic coma	0 (0.00%)	1 (0.55%)	1 (0.28%)

Ischaemic stroke	0 (0.00%)	1 (0.55%)	1 (0.28%)
Syncope	1 (0.56%)	1 (0.55%)	2 (0.56%)
Transient ischaemic attack	0 (0.00%)	2 (1.10%)	2 (0.56%)
Psychiatric disorders			
Depression	0 (0.00%)	1 (0.55%)	1 (0.28%)
Renal and urinary disorders			
Acute kidney injury	1 (0.56%)	0 (0.00%)	1 (0.28%)
Chronic kidney disease	0 (0.00%)	3 (1.66%)	3 (0.83%)
Diabetic nephropathy	1 (0.56%)	2 (1.10%)	3 (0.83%)
Dysuria	0 (0.00%)	1 (0.55%)	1 (0.28%)
Nephropathy	1 (0.56%)	0 (0.00%)	1 (0.28%)
Nephrotic syndrome	1 (0.56%)	0 (0.00%)	1 (0.28%)
Renal failure	0 (0.00%)	2 (1.10%)	2 (0.56%)
Urinary retention	0 (0.00%)	1 (0.55%)	1 (0.28%)
Reproductive system and breast disorders			
Breast hypoplasia	0 (0.00%)	1 (0.55%)	1 (0.28%)
Postmenopausal haemorrhage	0 (0.00%)	1 (0.55%)	1 (0.28%)
Respiratory, thoracic and mediastinal disorders			
Asthma	0 (0.00%)	1 (0.55%)	1 (0.28%)
Dyspnoea	0 (0.00%)	1 (0.55%)	1 (0.28%)
Hypoventilation	1 (0.56%)	0 (0.00%)	1 (0.28%)
Pulmonary embolism	0 (0.00%)	1 (0.55%)	1 (0.28%)
Pulmonary oedema	1 (0.56%)	0 (0.00%)	1 (0.28%)

Sleep apnoea syndrome	1 (0.56%)	0 (0.00%)	1 (0.28%)
Skin and subcutaneous tissue disorders			
Diabetic foot	0 (0.00%)	1 (0.55%)	1 (0.28%)
Vascular disorders			
Aortic stenosis	1 (0.56%)	0 (0.00%)	1 (0.28%)
Arterial stenosis	1 (0.56%)	0 (0.00%)	1 (0.28%)
Arteriovenous fistula	0 (0.00%)	1 (0.55%)	1 (0.28%)
Extremity necrosis	0 (0.00%)	2 (1.10%)	2 (0.56%)
Hypertension	1 (0.56%)	0 (0.00%)	1 (0.28%)
Peripheral arterial occlusive disease	0 (0.00%)	1 (0.55%)	1 (0.28%)
Peripheral ischaemia	1 (0.56%)	0 (0.00%)	1 (0.28%)

Other Adverse Events by System Organ Class

Time Frame	From first dose of study treatment up to 30 days after last dose (maximum 35 months)
Additional Description	Adverse Events (AEs) and All-cause mortality were collected in the Safety Set
Source Vocabulary for Table Default	MedDRA (24.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	2%

	Brolucizumab 6mg N = 179	**Aflibercept 2mg N = 181**	**Overall N = 360**
Arm/Group Description	Brolucizumab 6 mg/0.05 mL, 5 loading doses, with subsequent doses per protocol-specified maintenance schedule	Aflibercept 2 mg/0.05 mL, as labeled, 5 loading doses, with subsequent doses every 8 weeks	Overall

Total participants affected	131 (73.18%)	134 (74.03%)	265 (73.61%)
Blood and lymphatic system disorders			
Anaemia	8 (4.47%)	8 (4.42%)	16 (4.44%)
Eye disorders			
Blepharitis - Fellow eye	2 (1.12%)	5 (2.76%)	7 (1.94%)
Blepharitis - Study eye	2 (1.12%)	4 (2.21%)	6 (1.67%)
Cataract - Fellow eye	11 (6.15%)	16 (8.84%)	27 (7.50%)
Cataract - Study eye	12 (6.70%)	19 (10.50%)	31 (8.61%)
Conjunctival haemorrhage - Fellow eye	1 (0.56%)	9 (4.97%)	10 (2.78%)
Conjunctival haemorrhage - Study eye	9 (5.03%)	6 (3.31%)	15 (4.17%)
Diabetic retinal oedema - Fellow eye	18 (10.06%)	16 (8.84%)	34 (9.44%)
Diabetic retinopathy - Fellow eye	5 (2.79%)	1 (0.55%)	6 (1.67%)
Dry eye - Fellow eye	9 (5.03%)	7 (3.87%)	16 (4.44%)
Dry eye - Study eye	9 (5.03%)	9 (4.97%)	18 (5.00%)
Eye pain - Study eye	6 (3.35%)	4 (2.21%)	10 (2.78%)
Eye pruritus - Fellow eye	5 (2.79%)	0 (0.00%)	5 (1.39%)
Eye pruritus - Study eye	5 (2.79%)	0 (0.00%)	5 (1.39%)
Macular fibrosis - Fellow eye	2 (1.12%)	4 (2.21%)	6 (1.67%)
Macular oedema - Fellow eye	5 (2.79%)	3 (1.66%)	8 (2.22%)
Vision blurred - Fellow eye	0 (0.00%)	4 (2.21%)	4 (1.11%)
Vision blurred - Study eye	1 (0.56%)	5 (2.76%)	6 (1.67%)
Visual acuity reduced - Fellow eye	4 (2.23%)	3 (1.66%)	7 (1.94%)
Visual acuity reduced - Study eye	6 (3.35%)	6 (3.31%)	12 (3.33%)

Vitreous floaters - Study eye	4 (2.23%)	4 (2.21%)	8 (2.22%)
Vitreous haemorrhage - Fellow eye	5 (2.79%)	6 (3.31%)	11 (3.06%)
Vitreous haemorrhage - Study eye	2 (1.12%)	4 (2.21%)	6 (1.67%)
Gastrointestinal disorders			
Abdominal pain upper	4 (2.23%)	2 (1.10%)	6 (1.67%)
Diarrhoea	3 (1.68%)	7 (3.87%)	10 (2.78%)
Nausea	5 (2.79%)	5 (2.76%)	10 (2.78%)
Vomiting	0 (0.00%)	4 (2.21%)	4 (1.11%)
General disorders and administration site conditions			
Asthenia	3 (1.68%)	7 (3.87%)	10 (2.78%)
Chest pain	4 (2.23%)	1 (0.55%)	5 (1.39%)
Oedema peripheral	4 (2.23%)	2 (1.10%)	6 (1.67%)
Peripheral swelling	0 (0.00%)	4 (2.21%)	4 (1.11%)
Pyrexia	8 (4.47%)	5 (2.76%)	13 (3.61%)
Infections and infestations			
Bronchitis	7 (3.91%)	5 (2.76%)	12 (3.33%)
Conjunctivitis - Fellow eye	4 (2.23%)	2 (1.10%)	6 (1.67%)
Conjunctivitis - Study eye	6 (3.35%)	1 (0.55%)	7 (1.94%)
COVID-19	3 (1.68%)	4 (2.21%)	7 (1.94%)
Gastroenteritis	4 (2.23%)	0 (0.00%)	4 (1.11%)
Herpes zoster	2 (1.12%)	5 (2.76%)	7 (1.94%)
Influenza	7 (3.91%)	4 (2.21%)	11 (3.06%)
Nasopharyngitis	16 (8.94%)	17 (9.39%)	33 (9.17%)
Pulpitis dental	2 (1.12%)	4 (2.21%)	6 (1.67%)

Rhinitis	2 (1.12%)	4 (2.21%)	6 (1.67%)
Upper respiratory tract infection	5 (2.79%)	3 (1.66%)	8 (2.22%)
Urinary tract infection	5 (2.79%)	4 (2.21%)	9 (2.50%)
Investigations			
Blood creatinine increased	8 (4.47%)	2 (1.10%)	10 (2.78%)
Blood pressure increased	5 (2.79%)	4 (2.21%)	9 (2.50%)
Blood triglycerides increased	2 (1.12%)	6 (3.31%)	8 (2.22%)
Blood urea increased	3 (1.68%)	4 (2.21%)	7 (1.94%)
Glycosylated haemoglobin increased	7 (3.91%)	5 (2.76%)	12 (3.33%)
Intraocular pressure increased - Fellow eye	2 (1.12%)	5 (2.76%)	7 (1.94%)
Intraocular pressure increased - Study eye	6 (3.35%)	4 (2.21%)	10 (2.78%)
Protein urine present	4 (2.23%)	5 (2.76%)	9 (2.50%)
White blood cells urine positive	1 (0.56%)	4 (2.21%)	5 (1.39%)
Metabolism and nutrition disorders			
Gout	1 (0.56%)	7 (3.87%)	8 (2.22%)
Hyperlipidaemia	8 (4.47%)	2 (1.10%)	10 (2.78%)
Musculoskeletal and connective tissue disorders			
Arthralgia	4 (2.23%)	6 (3.31%)	10 (2.78%)
Back pain	7 (3.91%)	2 (1.10%)	9 (2.50%)
Pain in extremity	0 (0.00%)	4 (2.21%)	4 (1.11%)
Nervous system disorders			
Dizziness	1 (0.56%)	4 (2.21%)	5 (1.39%)

Headache	8 (4.47%)	4 (2.21%)	12 (3.33%)
Renal and urinary disorders			
Chronic kidney disease	4 (2.23%)	4 (2.21%)	8 (2.22%)
Diabetic nephropathy	5 (2.79%)	7 (3.87%)	12 (3.33%)
Proteinuria	6 (3.35%)	13 (7.18%)	19 (5.28%)
Reproductive system and breast disorders			
Benign prostatic hyperplasia	4 (2.23%)	3 (1.66%)	7 (1.94%)
Respiratory, thoracic and mediastinal disorders			
Cough	5 (2.79%)	10 (5.52%)	15 (4.17%)
Skin and subcutaneous tissue disorders			
Diabetic foot	4 (2.23%)	3 (1.66%)	7 (1.94%)
Vascular disorders			
Hypertension	15 (8.38%)	17 (9.39%)	32 (8.89%)
Peripheral arterial occlusive disease	4 (2.23%)	2 (1.10%)	6 (1.67%)

Other Relevant Findings

None

Conclusion:

Non-inferiority of brolucizumab 6 mg to aflibercept 2 mg was demonstrated on visual acuity for the primary endpoint and the first key secondary endpoint in this study in the year 1 analysis (Study B2302 Week 52 Interim CSR dated 08-Oct-2021). The overall results from the analysis at the end of year 2 for this study confirmed the results from the year 1 analysis in terms of the safety profile of brolucizumab as compared to the standard of care aflibercept and the sustained effects of the 4-week treatment interval extensions for brolucizumab over time resulting in fewer IVT injections.

- Brolucizumab 6 mg administered in a q6w regimen during the loading phase and q16w/q12w/q8w thereafter showed greater overall improvement compared to aflibercept 2 mg with respect to the anatomical outcomes.
- The high proportion (69.6%) of subjects who were identified as “no q8w treatment need” during the initial q12w cycle still receiving brolucizumab q12w or q16w during maintenance phase demonstrates the potential for brolucizumab to reduce patient burden based on durable disease control.
- A clinically relevant improvement in the proportion of subjects with >= 2-step and a >= 3-step improvement from baseline in the ETDRS DRSS score at Week 100 was observed with brolucizumab 6 mg and comparable to aflibercept.
- Subjects in the brolucizumab showed a higher improvement in visual functioning than the aflibercept arm assessed by the VFQ-25 questionnaire.
- The overall safety of brolucizumab was comparable to aflibercept over 2 years of treatment. Intraocular inflammation was reported in 2.2% of subjects in the brolucizumab arm and 1.7% in the aflibercept arm, of which no retinal vasculitis was reported in either arm, and retinal vascular occlusion was reported in 0.6% of subjects in both arms.
- The data from year 2 further strengthen the value of brolucizumab 6 mg as a new therapy for patients with visual impairment due to DME which can address the unmet medical need of long-acting effective disease control with reduced treatment and monitoring burden.

Date of Clinical Trial Report

08-Oct-2021	Week 52 Interim CSR
01-Feb-2022	Clinical Study Report