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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Brolucizumab/RTH258

Trial Indication(s)

Neovascular age-related macular degeneration (wet AMD)

Protocol Number

CRTH258A2303

Protocol Title

A 64-week, two-arm, randomized, double-masked, multicenter, phase IIIb study assessing the efficacy and safety of brolucizumab 6 mg compared to aflibercept 2 mg in a treat-to-control regimen in patients with neovascular agerelated macular degeneration (TALON)

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase IIIb

Study Start/End Dates

Study Start Date: September 25, 2019 (Actual)
Primary Completion Date: September 09, 2022 (Actual)

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Study Completion Date: September 09, 2022 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a 64-week, randomized, double-masked, multi-center, active-controlled, two-arm study in patients with confirmed neovascular age-related macular degeneration (nAMD) at screening who have not previously received anti-vascular endothelial growth factor (VEGF) treatment.

At the baseline Visit, subjects who met the eligibility criteria were randomized in a 1:1 ratio to receive either:

- Brolucizumab 6 mg: 3 × 4-week injections and one 8-week injection, followed by Treat-to-Control treatment from Week 16 up to Week 60/62
- Aflibercept 2 mg: 3 × 4-week injections and one 8-week injection, followed by Treat-to-Control treatment from Week 16 up to Week 60/62.

For all subjects, the last potential study treatment was at the Week 60 visit (or at the Week 62 visit for subjects whose actual treatment interval would require a treatment at Week 62). The initiation phase starts on Day 1 and ends on Week 16. Treat to Control regimen starts on Week 16 until end of treatment (Week 60/62).

In both treatment arms, treatment intervals after the initiation phase were either 8 weeks, 12 weeks, or 16 weeks. Per the original protocol, if it was determined that a patient required more frequent injections than every 8 weeks (q8w), he/she would be moved to a every 4 weeks (q4w) treatment interval. However, this option was removed per Protocol amendment 02, after which, dosing intervals shorter than q8w were not permitted.

At the investigator’s discretion, an inspection visit 6 weeks after the last injection could be performed when the injection interval was extended from 4 weeks to 8 weeks, i.e., after the 3rd injection at Week 8. If there was no disease activity in the study eye at the inspection visit, as assessed by the masked investigator, no treatment should be administered and the next visit and injection should take place 2 weeks later, i.e., 8 weeks after the previous study treatment. If disease activity was observed by the masked investigator in the study eye at the inspection visit at Week 14, the study treatment

should be administered by the unmasked investigator, and the subject should be discontinued from further study treatment at the next visit. Inspection visits 10 weeks and 14 weeks after the last injection could have been performed when the injection interval was extended from 8 weeks to 12 weeks, and from 12 weeks to 16 weeks, respectively.

Centers

119 centers in 20 countries: Australia(8), France(11), Korea, Republic of(6), Belgium(2), Czech Republic(5), Netherlands(2), Germany(11), Spain(9), Switzerland(1), Taiwan(4), Portugal(3), Sweden(2), Malaysia(3), Israel(4), Austria(2), United States(24), Canada(5), Argentina(4), United Kingdom(6), Italy(7)

Objectives:

Primary objectives:

- To demonstrate that brolucizumab is superior to aflibercept with respect to the duration of treatment intervals at Week 32
- To demonstrate that brolucizumab is non-inferior to aflibercept with respect to average change in best-corrected visual acuity (BCVA) from baseline at Weeks 28 and 32

Secondary objectives:

- To evaluate the durability of brolucizumab relative to aflibercept
- To evaluate the functional outcomes with brolucizumab relative to aflibercept
- To evaluate the anatomical outcomes with brolucizumab relative to aflibercept
- To evaluate the effect of brolucizumab relative to aflibercept on Patient-Reported Outcomes (PRO)
- To assess the safety and tolerability of brolucizumab relative to aflibercept

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

- Brolucizumab 6 mg: 3 × 4-week intravitreal injections and one 8-week Intravitreal injection, followed by Treat-to-Control treatment from Week 16 up to Week 60/62

- Aflibercept 2 mg: 3 × 4-week intravitreal injections and one 8-week Intravitreal injection, followed by Treat-to-Control treatment from Week 16 up to Week 60/62.

Statistical Methods

Efficacy:

Primary efficacy endpoints: The analyses of primacy endpoints were conducted using the full analysis set (FAS) population and repeated with the per-protocol set (PPS) population.

- To test the superiority of brolucizumab vs aflibercept in terms of the distribution of the last interval with no disease activity up to Week 32, a one-sided Wilcoxon test for 2 ordered multinomial distribution with type I error of $\alpha = 0.025$ was performed. The number (%) of subjects in q4w, q8w, and q12w at Week 32 together with the respective P-value of the Wilcoxon test was provided.
- To test the non-inferiority of brolucizumab compared to aflibercept in terms of average change in Best-corrected visual acuity (BCVA) from baseline at Week 28 and Week 32, a two-sided 95% confidence interval (CI) for the treatment difference was derived from an analysis of variance (ANOVA) model with treatment arm, baseline BCVA categories and age categories as fixed effects. To demonstrate the non-inferiority, the lower limit of the two-sided 95% CI for the treatment difference (brolucizumab – aflibercept) must be greater than -4 letters representing the non-inferiority margin. The respective one-sided p-value for non-inferiority in terms of change in BCVA assessed at significance level of 0.025 was also provided.

Secondary efficacy endpoints: No statistical hypotheses were tested for the secondary efficacy endpoints. The FAS was used for all secondary endpoints.

Secondary endpoints related to durability:

- Distribution of the last interval with no disease activity up to Week 64 for both arms was provided. Analysis was performed as per the primary endpoint (a one-sided Wilcoxon test with a p-value at 0.025 significance level was used).
- Distribution of the maximal interval with no disease activity up to Week 64 for both arms was provided. Analysis was performed as per the primary endpoint.
- Number (%) of subjects with no disease activity at Weeks 14 and 16 for both arms were provided. Odds ratio and 95% CI were provided.

- Time to first dry retina, defined as no intraretinal fluid (IRF) and no subretinal fluid (SRF), was analyzed using the Kaplan-Meier method.

Secondary endpoints related to functional outcomes:

- Average change in BCVA from baseline at Weeks 60 and 64.
- Summary statistics of average change in BCVA from baseline by visit per treatment arm was provided.
- Number (%) of subjects with occurrence of BCVA improvements of ≥5, ≥ 10, and ≥ 15 letters from baseline or BCVA ≥ 84 Letters at Week 32, Week 64 and the last injection visit per treatment arm was provided.
- Number (%) of subjects with occurrence of BCVA ≥ 69 letters at Week 32, Week 64 and the last injection visit per treatment arm was provided.

Secondary endpoints related to anatomical outcomes:

- Average change in central subfield thickness (CSFT) from baseline as assessed by spectral domain optical coherence tomography (SD-OCT) at Weeks 28 and 32 per treatment was provided.
- Average change in CSFT from baseline as assessed by SD-OCT at Weeks 60 and 64 per treatment arm was provided.
- A summary statistic of change in CSFT from baseline by visit was provided for both treatment arms.
- Number (%) of subjects with presence of IRF and/or SRF and sub-retinal pigment epithelium (RPE) fluid in the central subfield, as assessed by SD-OCT at Weeks 4, 8, 12, 16, 28 and 32, by visit and by number of visits (0, 1, 2 visits) per treatment arm was provided.
- Number (%) of subjects with presence of IRF and/or, SRF, and sub-RPE fluid in the central subfield, as assessed by SD-OCT at Weeks 60 and 64, by visit and by number of visits (0, 1, 2 visits) per treatment arm was provide.

The safety analyses were descriptive, no hypothesis testing was performed. Treatment-emergent ocular and non-ocular adverse events (AEs) were summarized by treatment arm. The number (%) of subjects with ocular adverse events of special interest (AESIs) in the study eye and other safety topics of interest were summarized by treatment, primary system organ class (for non-ocular AEs only) and preferred term.

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Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
-Signed informed consent must be obtained prior to participation in the study
-Male or female patients ≥ 50 years of age at screening who are treatment naive
-Active choroidal neovascularization (CNV) secondary to AMD that affects the central subfield, including retinal angiomatous proliferation (RAP) with a CNV component, confirmed by presence of active leakage from CNV seen by fluorescein angiography and sequellae of CNV, e.g. pigment epithelial detachment (PED), subretinal or sub-retinal pigment epithelium (sub-RPE) hemorrhage, blocked fluorescence, macular edema (study eye)
-Presence of intraretinal fluid (IRF) or subretinal fluid (SRF) that affects the central subfield, as seen by Spectral Domain Optical Coherence Tomography (SD-OCT) (study eye)
-Best-corrected visual acuity (BCVA) score between 83 and 38 letters, inclusive, using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at both screening and baseline visit (study eye)

Exclusion Criteria:
-Ocular conditions/disorders 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 planned medical or surgical intervention during the first 12-month study period, structural damage of the fovea, atrophy or fibrosis at the center of the fovea (study eye)
-Any active intraocular or periocular infection or active intraocular inflammation, at screening or baseline (study eye)
-Uncontrolled glaucoma defined as intraocular pressure (IOP) > 25 mmHg on medication, or according to investigator's judgment, at screening or baseline (study eye)
-Ocular treatments: previous treatment with any anti-vascular endothelial growth factor (VEGF) drugs or investigational drugs, intraocular or periocular steroids, macular laser photocoagulation, photodynamic therapy, vitreoretinal surgery, intraocular surgery (study eye)
-Stroke or myocardial infarction during the 6-month period prior to baseline
-Systemic anti-VEGF therapy at any time.

Participant Flow Table

Overall Study

	Brolucizumab 6 mg	Aflibercept 2 mg	Total
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection	

Started	366	368	734
Completed	317	307	624
Not Completed	49	61	110
Adverse Event	4	5	9
Death	4	2	6
Lost to Follow-up	6	2	8
Physician Decision	7	13	20
Protocol Violation	0	1	1
Withdrawal by Subject	28	38	66

Baseline Characteristics

	Brolucizumab 6 mg	**Aflibercept 2 mg**	**Total**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection	
Number of Participants [units: participants]	366	368	734
Baseline Analysis Population Description			
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation			
	75.5±7.85	75.5±8.41	75.5±8.13
Age Categorical (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
<=18 years	0	0	0

Between 18 and 65 years	32	37	69
>=65 years	334	331	665
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	216	204	420
Male	150	164	314
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
American Indian or Alaska Native	0	0	0
Asian	55	55	110
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	310	312	622
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Primary Outcome Result(s)

Distribution of the last interval with no disease activity up to Week 32 - study eye

Description: No disease activity is defined as no change in visual acuity and no change in other signs of the disease (e.g. Intraretinal Fluid (IRF), Subretinal Fluid (SRF), hemorrhage, leakage, etc.). Treatment interval distribution. Number (%) of subjects at 12/8/4-weeks intervals up to Week 32 for the study eye. If the study treatment is discontinued before Week 16, then the treatment interval is 4 weeks; otherwise. the last interval with no disease activity is used (if there was disease activity, the last interval is shortened by 4 weeks, down to a minimum of 4

weeks). If the duration of the last interval falls within the following ranges of (4-week, 8-week) or (8-week, 12-week) or ≥12-week then the floor value of these ranges was used.

Time Frame	Up to Week 32
Analysis Population Description	Full Analysis Set (Includes participants who were randomized and treated.)

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Distribution of the last interval with no disease activity up to Week 32 - study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
12 weeks	141 (38.52%)	73 (19.84%)
8 weeks	131 (35.79%)	147 (39.95%)
4 weeks	94 (25.68%)	148 (40.22%)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	
Type of Statistical Test	Superiority	
P Value	<0.0001	with significance level of 0.025
Method	Wilcoxon (Mann-Whitney)	

% Confidence Interval 1-Sided	to

Average change from baseline at Week 28 and Week 32 in Best-corrected visual acuity (BCVA) - study eye

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Min and max possible scores are 0-100 respectively. A higher score represents better visual functioning. Least squares mean estimate - for weeks 28 and 32 combined.
Time Frame	Baseline, Week 28 and Week 32
Analysis Population Description	Full Analysis Set - Last observation carried forward (LOCF).

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Average change from baseline at Week 28 and Week 32 in Best-corrected visual acuity (BCVA) - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	5.2 ± 0.51	5.1 ± 0.51

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Non-Inferiority
Non-Inferiority/Equivalence Test	4 letter margin (1-sided)
P Value	<0.0001

Method	ANOVA
Other Difference	0.1
Standard Error of the mean	0.73
95 % Confidence Interval 2-Sided	-1.3 to 1.5

Secondary Outcome Result(s)

Distribution of the last interval with no disease activity up to Week 64 - study eye

Description	No disease activity is defined as no change in visual acuity and no change in other signs of the disease (e.g. IRF, SRF, hemorrhage, leakage, etc.). Treatment interval distribution. The number of subjects at 16/12/8/4-weeks intervals as the last interval with no disease activity. If the study treatment is discontinued before Week 16, then the treatment interval is 4 weeks; otherwise. the last interval with no disease activity is used (if there was disease activity, the last interval is shortened by 4 weeks, down to a minimum of 4 weeks). If the duration of the last interval falls within the following ranges of (4-week, 8-week) or (8-week, 12-week) or (12-weeks, 16-weeks) or ≥16-week then the floor value of these ranges was used.
Time Frame	Up to Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Distribution of the last interval with no disease activity up to Week 64 - study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**

16 Weeks	104 (28.42%)	45 (12.23%)
12 Weeks	82 (22.4%)	88 (23.91%)
8 Weeks	95 (25.96%)	81 (22.01%)
4 Weeks	85 (23.22%)	154 (41.85%)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
P Value	<0.0001
Method	Wilcoxon (Mann-Whitney)
% Confidence Interval 1-Sided	to

Distribution of the maximal intervals with no disease activity up to Week 64 - study eye

Description	No disease activity is defined as no change in visual acuity and no change in other signs of the disease (e.g. IRF, SRF, hemorrhage, leakage, etc.). Maximal interval distribution. Number of subjects at 16/12/8/4-weeks intervals as the last interval with no disease activity. If the study treatment is discontinued before Week 16 included, then the treatment interval is 4 weeks; otherwise, the last interval with no disease activity is used (if there was disease activity, the last interval is shortened by 4 weeks, down to a minimum of 4 weeks). If the duration of the maximal interval falls within the following ranges of [4-weeks, 8-weeks) or [8-weeks, 12-weeks) or [12-weeks, 16-weeks] or ≥16-weeks then the floor value of these ranges is used.
Time Frame	Up to Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Distribution of the maximal intervals with no disease activity up to Week 64 - study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
16 Weeks	117 (31.97%)	57 (15.49%)
12 Weeks	96 (26.23%)	92 (25%)
8 Weeks	94 (25.68%)	114 (30.98%)
4 Weeks	59 (16.12%)	105 (28.53%)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
P Value	<0.0001
Method	Wilcoxon (Mann-Whitney)

Number of participants with no disease activity - study eye

Description	Disease activity assessment as determined by visual acuity and assessment of other signs of the disease (e.g. IRF, SRF, hemorrhage, leakage, etc.).
Time Frame	Weeks 14 and 16
Analysis Population Description	Full Analysis Set. Note that the number analyzed is reduced because the Week 14 visit was conducted at the investigator's discretion, and because some patients had already stopped treatment by Week 16.

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	301	296
Number of participants with no disease activity - study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Week 14 (n=118, 137)	87 (73.73%)	88 (64.23%)
Week 16 (n=301,296)	260 (86.38%)	211 (71.28%)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	
Type of Statistical Test	Superiority	
Non-Inferiority/Equivalence Test	Week 14	
P Value	0.0510	
Method	Other likelihood ratio test	Assessed at one-sided 0.025 significance level
Odds Ratio (OR)	1.6	
95 % Confidence Interval 2-Sided	0.9 to 2.7	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg

Type of Statistical Test	Superiority	
Non-Inferiority/Equivalence Test	Week 16	
P Value	<0.0001	
Method	Other likelihood ratio test	Assessed at one-sided 0.025 significance level
Odds Ratio (OR)	2.6	
95 % Confidence Interval 2-Sided	1.7 to 3.9	

Time from Last Loading Injection to First Visit with No Disease Activity (Weeks) - 75th percentile - study eye

Description	Intraretinal fluid (IRF) and subretinal fluid (SRF) were assessed by Spectral Domain Optical Coherence Tomography (SD-OCT) (study eye). Please note that this endpoint can be impacted by the optional disease activity assessment visits and the flexible dosing regimen, in addition to the randomized treatment. Hence, the observed treatment effect may be confounded by the study design artifacts.
Time Frame	Up to Week 64
Analysis Population Description	Full Analysis Set – subjects with no important protocol deviations with impact

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Time from Last Loading Injection to First Visit with No Disease Activity (Weeks) - 75th percentile - study eye (units: weeks)	**Number** **(95% Confidence Interval)**	**Number** **(95% Confidence Interval)**
75th percentile	9.1 (8.9 to 10.6)	12.1 (11.3 to 12.9)

Time-to-first dry retina - time to the first visit with no Intraretinal Fluid (IRF) or Subretinal Fluid (SRF) - study eye

Description	Intraretinal fluid (IRF) and subretinal fluid (SRF) were assessed by Spectral Domain Optical Coherence Tomography (SD-OCT) (study eye).
Time Frame	Up to Week 64
Analysis Population Description	Full Analysis Set – subjects with no important protocol deviations with impact

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	330	337
Time-to-first dry retina - time to the first visit with no Intraretinal Fluid (IRF) or Subretinal Fluid (SRF) - study eye (units: Participants)		
0 Week	330	337
4 Week	144	138
8 Week	70	86
12 Week	70	86
16 Week	37	67
20 Week	34	55
24 Week	30	47
28 Week	28	38
32 Week	20	25
36 Week	20	23
40 Week	18	22
44 Week	18	22

48 Week	17	20
52 Week	17	20
56 Week	17	20
60 Week	11	14
64 Week	0	0

Average change from baseline at Week 60 and Week 64 in Best-corrected visual acuity (BCVA) - study eye

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Min and max possible scores are 0-100 respectively. A higher score represents better visual functioning. Least squares mean estimate - for weeks 60 and 64 combined.
Time Frame	Baseline, Week 60 and Week 64
Analysis Population Description	Full Analysis Set - LOCF

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Average change from baseline at Week 60 and Week 64 in Best-corrected visual acuity (BCVA) - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
	4.7 ± 0.60	4.9 ± 0.60

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg

Type of Statistical Test	Superiority	
P Value	0.8137	p-value for treatment difference
Method	ANOVA	
Other Difference	-0.2	
Standard Error of the mean	0.84	
95 % Confidence Interval 2-Sided	-1.9 to 1.5	

Number of participants with best-corrected visual acuity improvements of ≥ 15 letters in BCVA from baseline or reached BCVA ≥ 84 letters up to Week 32/64 per treatment arm - study eye

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Min and max possible scores are 0-100 respectively. A higher score represents better visual functioning.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set – LOCF

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Number of participants with best-corrected visual acuity improvements of ≥ 15 letters in BCVA from baseline or reached BCVA ≥ 84 letters up to Week 32/64 per treatment arm - study eye (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Week 32	88 (24.04%)	92 (25%)

Week 64	89 (24.32%)	91 (24.73%)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	
Type of Statistical Test	Superiority	
Non-Inferiority/Equivalence Test	Week 32	
P Value	0.4106	
Method	Other likelihood ratio test	adjusting for baseline BCVA categories (<55, 55-<73, ≥73 letters).
Odds Ratio (OR)	1.0	
95 % Confidence Interval 2-Sided	0.7 to 1.3	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	
Type of Statistical Test	Superiority	
Non-Inferiority/Equivalence Test	Week 64	
P Value	0.4667	
Method	Other likelihood ratio test	adjusting for baseline BCVA categories (<55, 55-<73, ≥73 letters).
Odds Ratio (OR)	1.0	

95 % Confidence Interval 2-Sided	0.7 to 1.4

Number of participants with best-corrected visual acuity ≥ 69 letters - study eye

Description	BCVA was assessed using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts. Min and max possible scores are 0-100 respectively. A higher score represents better visual functioning.
Time Frame	Week 32 and Week 64
Analysis Population Description	Full Analysis Set - LOCF

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Number of participants with best-corrected visual acuity ≥ 69 letters - study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Week 32	244 (66.67%)	228 (61.96%)
Week 64	240 (65.57%)	219 (59.51%)

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32

P Value	0.2397	
Method	Other likelihood ratio test	assessed at the 0.025 significance level
Odds Ratio (OR)	1.1	
95 % Confidence Interval 2-Sided	0.8 to 1.7	

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg	
Type of Statistical Test	Superiority	
Non-Inferiority/Equivalence Test	Week 64	
P Value	0.1150	
Method	Other likelihood ratio test	assessed at the 0.025 significance level
Odds Ratio (OR)	1.2	
95 % Confidence Interval 2-Sided	0.9 to 1.8	

Average change from baseline in Central Subfield Thickness (CSFT) - study eye

Description	CSFT was measured by Spectral Domain Optical Coherence Tomography
Time Frame	Baseline, Weeks 28 and 32 and at Weeks 60 and 64
Analysis Population Description	Full Analysis Set - LOCF

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Average change from baseline in Central Subfield Thickness (CSFT) - study eye (units: micrometers)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Weeks 28 and 32 (average)	-166.9 ± 6.97	-140.0 ± 6.96
Weeks 60 and 64 (average)	-182.9 ± 7.72	-167.5 ± 8.16

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Weeks 28 and 32
P Value	0.0066
Method	ANOVA
Other Difference	-26.9
Standard Error of the mean	9.87
95 % Confidence Interval 2-Sided	-46.3 to -7.5

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg

Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Weeks 60 and 64
P Value	0.1714
Method	ANOVA
Other Difference	-15.4
Standard Error of the mean	11.26
95 % Confidence Interval 2-Sided	-37.6 to 6.7

Number of participants with presence of Intraretinal Fluid and/or Subretinal Fluid in the central subfield - study eye

Description	Intraretinal Fluid and/or Subretinal Fluid status was measured by Spectral Domain Optical Coherence Tomography (SD-OCT).
Time Frame	At Weeks 28, 32, 60 and 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	286	289
Number of participants with presence of Intraretinal Fluid and/or Subretinal Fluid in the central subfield - study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Week 28 (n=285,289)	175 (61.4%)	198 (68.51%)

Week 32 (n=286, 267)	144 (50.35%)	152 (56.93%)
Week 60 (n=269,244)	60 (22.3%)	69 (28.28%)
Week 64 (n=271, 241)	72 (26.57%)	83 (34.44%)

Number of participants with presence of sub-Retinal Pigment Epithelium fluid in the central subfield - study eye

Description	Sub-Retinal Pigment Epithelium fluid status was measured by Spectral Domain Optical Coherence Tomography (SD-OCT).
Time Frame	At Weeks 28, 32, 60 and 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	288	289
Number of participants with presence of sub-Retinal Pigment Epithelium fluid in the central subfield - study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Week 28 (n=288,289)	173 (60.07%)	208 (71.97%)
Week 32 (n=288, 266)	156 (54.17%)	175 (65.79%)
Week 60 (n=271,244)	27 (9.96%)	31 (12.7%)
Week 64 (n=271, 242)	34 (12.55%)	43 (17.77%)

NOVARTIS

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - Composite scores - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - Composite scores - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	4.09 ± 0.20	3.72 ± 0.21
Week 64 (n=248, 224)	2.8 ± 0.69	4.7 ± 0.73

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.193

Method	ANCOVA
Other LS Mean Difference	0.37
95 % Confidence Interval 2-Sided	-0.2 to 0.9

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.052
Method	ANCOVA
Other LS Mean Difference	-2.0
95 % Confidence Interval 2-Sided	-3.9 to 0.0

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - General Vision - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64

NOVARTIS

Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - General Vision - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	7.94 ± 0.86	5.79 ± 0.89
Week 64 (n=248, 224)	7.3 ± 0.87	8.0 ± 0.92

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.081
Method	ANCOVA
Other LS Mean Difference	2.16
95 % Confidence Interval 2-Sided	-0.3 to 4.6

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.590
Method	ANCOVA
Other LS Mean Difference	-0.7
95 % Confidence Interval 2-Sided	-3.2 to 1.8

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Ocular Pain - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection

Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Ocular Pain - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	3.55 ± 0.92	2.78 ± 0.94
Week 64 (n=248, 224)	3.1 ± 0.89	5.0 ± 0.94

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.558
Method	ANCOVA
Other LS Mean Difference	0.77
95 % Confidence Interval 2-Sided	-1.8 to 3.4

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.138

Method	ANCOVA
Other LS Mean Difference	-1.9
95 % Confidence Interval 2-Sided	-4.5 to 0.6

Change from baseline n Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Near Activities - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline n Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Near Activities - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	7.46 ± 1.05	5.86 ± 1.08
Week 64 (n=248, 224)	4.9 ± 1.12	7.9 ± 1.18

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.287
Method	ANCOVA
Other LS Mean Difference	1.60
95 % Confidence Interval 2-Sided	-1.4 to 4.6

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.070
Method	ANCOVA
Other LS Mean Difference	-3.0
95 % Confidence Interval 2-Sided	-6.2 to 0.2

NOVARTIS

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Distance Activities - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Distance Activities - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	3.06 ± 0.95	3.78 ± 0.98
Week 64 (n=248, 224)	2.5 ± 0.99	5.0 ± 1.04

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.602

Method	ANCOVA
Other LS Mean Difference	-0.71
95 % Confidence Interval 2-Sided	-3.4 to 2.0

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.086
Method	ANCOVA
Other LS Mean Difference	-2.5
95 % Confidence Interval 2-Sided	-5.3 to 0.4

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Social Functioning - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning or outcome. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64

Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Social Functioning - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	1.99 ± 0.79	0.43 ± 0.82
Week 64 (n=247, 223)	0.2 ± 0.81	1.7 ± 0.85

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.174
Method	ANCOVA
Other LS Mean Difference	1.55
95 % Confidence Interval 2-Sided	-0.7 to 3.8

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Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.210
Method	ANCOVA
Other LS Mean Difference	-1.5
95 % Confidence Interval 2-Sided	-3.8 to 0.8

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Mental Health - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning or outcome. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection

Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Mental Health - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	5.83 ± 0.99	6.79 ± 1.02
Week 64 (n=248, 224)	5.0 ± 1.08	7.2 ± 1.14

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.499
Method	ANCOVA
Other LS Mean Difference	-0.96
95 % Confidence Interval 2-Sided	-3.8 to 1.8

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.147

Method	ANCOVA
Other LS Mean Difference	-2.3
95 % Confidence Interval 2-Sided	-5.4 to 0.8

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Role Difficulties - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning or outcome. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Role Difficulties - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	5.17 ± 1.31	4.30 ± 1.35
Week 64 (n=248, 224)	4.7 ± 1.31	5.9 ± 1.38

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.643
Method	ANCOVA
Other LS Mean Difference	0.88
95 % Confidence Interval 2-Sided	-2.8 to 4.6

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.507
Method	ANCOVA
Other LS Mean Difference	-1.3
95 % Confidence Interval 2-Sided	-5.0 to 2.5

NOVARTIS

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Dependency - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning or outcome. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Dependency - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	2.71 ± 0.88	2.22 ± 0.91
Week 64 (n=248, 224)	-0.6 ± 1.09	2.2 ± 1.14

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.700

Method	ANCOVA
Other LS Mean Difference	0.49
95 % Confidence Interval 2-Sided	-2.0 to 3.0

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.070
Method	ANCOVA
Other LS Mean Difference	-2.9
95 % Confidence Interval 2-Sided	-6.0 to 0.2

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Driving - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64

Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Driving - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	4.92 ± 1.56	4.19 ± 1.57
Week 64 (n=139, 131)	1.3 ± 1.74	3.0 ± 1.79

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.741
Method	ANCOVA
Other LS Mean Difference	0.73
95 % Confidence Interval 2-Sided	-3.6 to 5.1

NOVARTIS

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.494
Method	ANCOVA
Other LS Mean Difference	-1.7
95 % Confidence Interval 2-Sided	-6.6 to 3.2

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Color Vision - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	Aflibercept 2 mg
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection

Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Color Vision - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	1.78 ± 0.63	0.02 ± 0.65
Week 64 (n=244, 222)	0.1 ± 0.80	1.2 ± 0.84

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.054
Method	ANCOVA
Other LS Mean Difference	1.76
95 % Confidence Interval 2-Sided	-0.0 to 3.5

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.331

Method	ANCOVA
Other LS Mean Difference	-1.1
95 % Confidence Interval 2-Sided	-3.4 to 1.2

Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Peripheral Vision - study eye

Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures the influence of visual disability and visual symptoms on general health domains. The NEI VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. All items are scored so that a high score represents better visual functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. Each subscale score has a range of 0 to 100 inclusive and will be calculated from the re-scaled raw data. A composite score is derived based on the average of the 11 subscales.
Time Frame	Baseline, Week 32, and Week 64
Analysis Population Description	Full Analysis Set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	278	261
Change from baseline in Visual Function Questionnnaire-25 (VFQ-25) - subscale score - Peripheral Vision - study eye (units: Scores on a scale)	**Least Squares Mean ± Standard Error**	**Least Squares Mean ± Standard Error**
Week 32 (n-278, 261)	3.24 ± 1.01	2.00 ± 1.04
Week 64 (n=243, 224)	2.5 ± 1.08	3.0 ± 1.13

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 32
P Value	0.394
Method	ANCOVA
Other LS Mean Difference	1.24
95 % Confidence Interval 2-Sided	-1.6 to 4.1

Statistical Analysis

Groups	Brolucizumab 6 mg, Aflibercept 2 mg
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 64
P Value	0.728
Method	ANCOVA
Other LS Mean Difference	-0.5
95 % Confidence Interval 2-Sided	-3.6 to 2.5

NOVARTIS

Number of participants with treatment emergent ocular adverse events (greater than or equal to 1% in any treatment arm) by preferred term for the study eye

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease) in a subject or clinical investigation subject.
Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of 483 days, approx. 69 weeks, 1.3 years.
Analysis Population Description	Safety Analysis set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Number of participants with treatment emergent ocular adverse events (greater than or equal to 1% in any treatment arm) by preferred term for the study eye (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Number of subjects with at least one event	114 (31.15%)	102 (27.72%)
Conjunctival haemorrhage	23 (6.28%)	13 (3.53%)
Visual acuity reduced	16 (4.37%)	18 (4.89%)
Eye pain	17 (4.64%)	13 (3.53%)
Vitreous floaters	12 (3.28%)	6 (1.63%)
Intraocular pressure increased	5 (1.37%)	11 (2.99%)
Subretinal fluid	5 (1.37%)	11 (2.99%)

Vitreous detachment	10 (2.73%)	3 (.82%)
Retinal haemorrhage	4 (1.09%)	7 (1.9%)
Cataract	5 (1.37%)	5 (1.36%)
Foreign body sensation in eyes	4 (1.09%)	6 (1.63%)
Intra-ocular injection complication	6 (1.64%)	3 (.82%)
Retinal pigment epithelial tear	5 (1.37%)	4 (1.09%)
Macular oedema	3 (.82%)	4 (1.09%)
Posterior capsule opacification	2 (.55%)	5 (1.36%)
Dry eye	2 (.55%)	4 (1.09%)
Hordeolum	4 (1.09%)	2 (.54%)
Neovascular age-related macular degeneration	2 (.55%)	4 (1.09%)
Retinal oedema	1 (.27%)	4 (1.09%)
Uveitis	4 (1.09%)	1 (.27%)
Vision blurred	4 (1.09%)	1 (.27%)
Detachment of retinal pigment epithelium	0 (%)	4 (1.09%)
Retinal artery occlusion	4 (1.09%)	0 (%)

Subretinal fibrosis	4 (1.09%)	0 (%)

Number of participants with treatment emergent non-ocular adverse events (greater than or equal to 2% in any treatment arm) - summary table

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease) in a subject or clinical investigation subject.
Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of 483 days, approx. 69 weeks, 1.3 years.
Analysis Population Description	Safety Analysis set

	Brolucizumab 6 mg	**Aflibercept 2 mg**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection
Number of Participants Analyzed [units: participants]	366	368
Number of participants with treatment emergent non-ocular adverse events (greater than or equal to 2% in any treatment arm) - summary table (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Number of subjects with at least one event	182 (49.73%)	185 (50.27%)

Safety Results

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of 483 days, approx. 69 weeks, 1.3 years.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Brolucizumab 6mg N = 366	**Aflibercept 2mg N = 368**	**All Patients N = 734**
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection	All Patients
Total Number Affected	4	2	6
Total Number At Risk	366	368	734

Serious Adverse Events

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of 483 days, approx. 69 weeks, 1.3 years.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

	Brolucizumab 6mg N = 366	Aflibercept 2mg N = 368	All Patients N = 734
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection	All Patients
Total # Affected by any Serious Adverse Event	58	53	111
Total # at Risk by any Serious Adverse Event	366	368	734
Blood and lymphatic system disorders			
Iron deficiency anaemia	1 (0.27%)	0 (0.00%)	1 (0.14%)
Cardiac disorders			
Acute myocardial infarction	1 (0.27%)	2 (0.54%)	3 (0.41%)
Angina pectoris	1 (0.27%)	0 (0.00%)	1 (0.14%)
Arrhythmia	0 (0.00%)	1 (0.27%)	1 (0.14%)
Atrial fibrillation	2 (0.55%)	0 (0.00%)	2 (0.27%)
Atrial flutter	1 (0.27%)	0 (0.00%)	1 (0.14%)
Cardiac arrest	1 (0.27%)	0 (0.00%)	1 (0.14%)
Cardiac failure	3 (0.82%)	1 (0.27%)	4 (0.54%)
Cardiac failure congestive	2 (0.55%)	0 (0.00%)	2 (0.27%)
Coronary artery disease	0 (0.00%)	1 (0.27%)	1 (0.14%)
Coronary artery stenosis	1 (0.27%)	0 (0.00%)	1 (0.14%)
Myocardial infarction	2 (0.55%)	1 (0.27%)	3 (0.41%)
Myocardial ischaemia	0 (0.00%)	1 (0.27%)	1 (0.14%)
Sinus node dysfunction	1 (0.27%)	0 (0.00%)	1 (0.14%)
Tachycardia	1 (0.27%)	0 (0.00%)	1 (0.14%)
Ear and labyrinth disorders			
Vertigo positional	1 (0.27%)	0 (0.00%)	1 (0.14%)

Eye disorders			
Eye inflammation - Study Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Glaucoma - Study Eye	0 (0.00%)	1 (0.27%)	1 (0.14%)
Iridocyclitis - Study Eye	1 (0.27%)	1 (0.27%)	2 (0.27%)
Macular hole - Study Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Ocular discomfort - Fellow Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Ocular discomfort - Study Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Retinal artery occlusion - Study Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Retinal vascular occlusion - Study Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Retinal vein occlusion - Study Eye	0 (0.00%)	1 (0.27%)	1 (0.14%)
Uveitis - Study Eye	3 (0.82%)	0 (0.00%)	3 (0.41%)
Visual acuity reduced - Study Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Gastrointestinal disorders			
Abdominal adhesions	0 (0.00%)	1 (0.27%)	1 (0.14%)
Gingival bleeding	1 (0.27%)	0 (0.00%)	1 (0.14%)
Ileus paralytic	0 (0.00%)	1 (0.27%)	1 (0.14%)
Inguinal hernia	1 (0.27%)	0 (0.00%)	1 (0.14%)
General disorders and administration site conditions			
Chest discomfort	0 (0.00%)	1 (0.27%)	1 (0.14%)
Hepatobiliary disorders			
Cholecystitis	1 (0.27%)	0 (0.00%)	1 (0.14%)
Immune system disorders			
Anaphylactic shock	1 (0.27%)	0 (0.00%)	1 (0.14%)

Infections and infestations			
COVID-19	2 (0.55%)	0 (0.00%)	2 (0.27%)
COVID-19 pneumonia	5 (1.37%)	1 (0.27%)	6 (0.82%)
Diverticulitis	0 (0.00%)	2 (0.54%)	2 (0.27%)
Endophthalmitis - Study Eye	1 (0.27%)	0 (0.00%)	1 (0.14%)
Erysipelas	1 (0.27%)	0 (0.00%)	1 (0.14%)
Escherichia sepsis	0 (0.00%)	1 (0.27%)	1 (0.14%)
Herpes zoster	1 (0.27%)	0 (0.00%)	1 (0.14%)
Pneumonia	2 (0.55%)	0 (0.00%)	2 (0.27%)
Pneumonia viral	0 (0.00%)	1 (0.27%)	1 (0.14%)
Pyelonephritis	0 (0.00%)	1 (0.27%)	1 (0.14%)
Urosepsis	0 (0.00%)	1 (0.27%)	1 (0.14%)
Injury, poisoning and procedural complications			
Cervical vertebral fracture	1 (0.27%)	1 (0.27%)	2 (0.27%)
Concussion	0 (0.00%)	1 (0.27%)	1 (0.14%)
Craniocerebral injury	1 (0.27%)	0 (0.00%)	1 (0.14%)
Face injury	0 (0.00%)	1 (0.27%)	1 (0.14%)
Facial bones fracture	0 (0.00%)	1 (0.27%)	1 (0.14%)
Fall	0 (0.00%)	2 (0.54%)	2 (0.27%)
Femoral neck fracture	2 (0.55%)	1 (0.27%)	3 (0.41%)
Femur fracture	0 (0.00%)	2 (0.54%)	2 (0.27%)
Foot fracture	1 (0.27%)	0 (0.00%)	1 (0.14%)
Forearm fracture	1 (0.27%)	0 (0.00%)	1 (0.14%)
Hip fracture	1 (0.27%)	1 (0.27%)	2 (0.27%)
Incisional hernia	1 (0.27%)	0 (0.00%)	1 (0.14%)

Meniscus injury	0 (0.00%)	1 (0.27%)	1 (0.14%)
Radius fracture	1 (0.27%)	1 (0.27%)	2 (0.27%)
Stress fracture	0 (0.00%)	1 (0.27%)	1 (0.14%)
Thoracic vertebral fracture	1 (0.27%)	0 (0.00%)	1 (0.14%)
Wrist fracture	2 (0.55%)	0 (0.00%)	2 (0.27%)
Investigations			
Intraocular pressure increased - Study Eye	0 (0.00%)	1 (0.27%)	1 (0.14%)
Metabolism and nutrition disorders			
Cachexia	1 (0.27%)	0 (0.00%)	1 (0.14%)
Hyperkalaemia	1 (0.27%)	0 (0.00%)	1 (0.14%)
Hyponatraemia	0 (0.00%)	1 (0.27%)	1 (0.14%)
Musculoskeletal and connective tissue disorders			
Neck pain	1 (0.27%)	1 (0.27%)	2 (0.27%)
Osteoarthritis	1 (0.27%)	1 (0.27%)	2 (0.27%)
Spinal stenosis	1 (0.27%)	0 (0.00%)	1 (0.14%)
Spondylolisthesis	0 (0.00%)	1 (0.27%)	1 (0.14%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric	1 (0.27%)	0 (0.00%)	1 (0.14%)
Anal cancer	0 (0.00%)	1 (0.27%)	1 (0.14%)
Breast cancer	1 (0.27%)	1 (0.27%)	2 (0.27%)
Colon cancer	1 (0.27%)	2 (0.54%)	3 (0.41%)
Hepatic cancer	1 (0.27%)	0 (0.00%)	1 (0.14%)
Lung neoplasm	1 (0.27%)	1 (0.27%)	2 (0.27%)
Metastatic squamous cell carcinoma	1 (0.27%)	0 (0.00%)	1 (0.14%)

Neoplasm	0 (0.00%)	1 (0.27%)	1 (0.14%)
Non-small cell lung cancer metastatic	1 (0.27%)	0 (0.00%)	1 (0.14%)
Pancreatic carcinoma	0 (0.00%)	1 (0.27%)	1 (0.14%)
Renal neoplasm	0 (0.00%)	1 (0.27%)	1 (0.14%)
Squamous cell carcinoma	0 (0.00%)	1 (0.27%)	1 (0.14%)
Tongue neoplasm malignant stage unspecified	1 (0.27%)	0 (0.00%)	1 (0.14%)
Nervous system disorders			
Basal ganglia infarction	1 (0.27%)	0 (0.00%)	1 (0.14%)
Carotid artery stenosis	1 (0.27%)	0 (0.00%)	1 (0.14%)
Cerebral infarction	0 (0.00%)	1 (0.27%)	1 (0.14%)
Cerebrovascular accident	0 (0.00%)	1 (0.27%)	1 (0.14%)
Dizziness	0 (0.00%)	1 (0.27%)	1 (0.14%)
Speech disorder	0 (0.00%)	1 (0.27%)	1 (0.14%)
Transient ischaemic attack	1 (0.27%)	0 (0.00%)	1 (0.14%)
Psychiatric disorders			
Abnormal behaviour	0 (0.00%)	1 (0.27%)	1 (0.14%)
Psychotic disorder due to a general medical condition	0 (0.00%)	1 (0.27%)	1 (0.14%)
Renal and urinary disorders			
Acute kidney injury	0 (0.00%)	1 (0.27%)	1 (0.14%)
Haematuria	0 (0.00%)	1 (0.27%)	1 (0.14%)
Nephrolithiasis	1 (0.27%)	0 (0.00%)	1 (0.14%)
Ureterolithiasis	0 (0.00%)	1 (0.27%)	1 (0.14%)
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure	0 (0.00%)	1 (0.27%)	1 (0.14%)

Dyspnoea exertional	1 (0.27%)	0 (0.00%)	1 (0.14%)
Epistaxis	1 (0.27%)	0 (0.00%)	1 (0.14%)
Hypercapnia	1 (0.27%)	0 (0.00%)	1 (0.14%)
Pneumonitis	1 (0.27%)	0 (0.00%)	1 (0.14%)
Pulmonary embolism	0 (0.00%)	2 (0.54%)	2 (0.27%)
Pulmonary oedema	0 (0.00%)	1 (0.27%)	1 (0.14%)
Vascular disorders			
Aortic stenosis	1 (0.27%)	1 (0.27%)	2 (0.27%)
Deep vein thrombosis	0 (0.00%)	1 (0.27%)	1 (0.14%)
Hypertensive crisis	0 (0.00%)	1 (0.27%)	1 (0.14%)
Peripheral arterial occlusive disease	0 (0.00%)	1 (0.27%)	1 (0.14%)
Peripheral artery aneurysm rupture	0 (0.00%)	1 (0.27%)	1 (0.14%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of 483 days, approx. 69 weeks, 1.3 years.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 1%

	Brolucizumab 6mg N = 366	Aflibercept 2mg N = 368	All Patients N = 734
Arm/Group Description	Intra-vitreal injection	Intra-vitreal injection	All Patients
Total # Affected by any Other Adverse Event	172	177	349
Total # at Risk by any Other Adverse Event	366	368	734
Blood and lymphatic system disorders			
Anaemia	0 (0.00%)	4 (1.09%)	4 (0.54%)
Cardiac disorders			
Atrial fibrillation	6 (1.64%)	1 (0.27%)	7 (0.95%)
Ear and labyrinth disorders			
Vertigo	4 (1.09%)	4 (1.09%)	8 (1.09%)
Eye disorders			
Cataract - Study Eye	5 (1.37%)	7 (1.90%)	12 (1.63%)
Choroidal neovascularisation - Fellow Eye	5 (1.37%)	7 (1.90%)	12 (1.63%)
Conjunctival haemorrhage - Fellow Eye	3 (0.82%)	4 (1.09%)	7 (0.95%)
Conjunctival haemorrhage - Study Eye	23 (6.28%)	13 (3.53%)	36 (4.90%)
Detachment of retinal pigment epithelium - Study Eye	0 (0.00%)	4 (1.09%)	4 (0.54%)
Dry eye - Fellow Eye	6 (1.64%)	16 (4.35%)	22 (3.00%)
Dry eye - Study Eye	8 (2.19%)	18 (4.89%)	26 (3.54%)
Eye pain - Fellow Eye	2 (0.55%)	4 (1.09%)	6 (0.82%)
Eye pain - Study Eye	17 (4.64%)	13 (3.53%)	30 (4.09%)

Eye pruritus - Study Eye	4 (1.09%)	1 (0.27%)	5 (0.68%)
Foreign body sensation in eyes - Study Eye	5 (1.37%)	8 (2.17%)	13 (1.77%)
Lacrimation increased - Fellow Eye	1 (0.27%)	4 (1.09%)	5 (0.68%)
Macular oedema - Study Eye	3 (0.82%)	4 (1.09%)	7 (0.95%)
Neovascular age-related macular degeneration - Fellow Eye	22 (6.01%)	17 (4.62%)	39 (5.31%)
Neovascular age-related macular degeneration - Study Eye	3 (0.82%)	4 (1.09%)	7 (0.95%)
Posterior capsule opacification - Study Eye	3 (0.82%)	5 (1.36%)	8 (1.09%)
Retinal depigmentation - Study Eye	1 (0.27%)	4 (1.09%)	5 (0.68%)
Retinal haemorrhage - Study Eye	4 (1.09%)	7 (1.90%)	11 (1.50%)
Retinal oedema - Study Eye	1 (0.27%)	4 (1.09%)	5 (0.68%)
Retinal pigment epithelial tear - Study Eye	5 (1.37%)	4 (1.09%)	9 (1.23%)
Subretinal fibrosis - Study Eye	4 (1.09%)	0 (0.00%)	4 (0.54%)
Subretinal fluid - Study Eye	5 (1.37%)	11 (2.99%)	16 (2.18%)
Vision blurred - Study Eye	4 (1.09%)	1 (0.27%)	5 (0.68%)
Visual acuity reduced - Fellow Eye	4 (1.09%)	4 (1.09%)	8 (1.09%)
Visual acuity reduced - Study Eye	18 (4.92%)	19 (5.16%)	37 (5.04%)
Vitreous detachment - Fellow Eye	5 (1.37%)	1 (0.27%)	6 (0.82%)
Vitreous detachment - Study Eye	11 (3.01%)	3 (0.82%)	14 (1.91%)
Vitreous floaters - Study Eye	14 (3.83%)	6 (1.63%)	20 (2.72%)
Gastrointestinal disorders			
Constipation	4 (1.09%)	0 (0.00%)	4 (0.54%)
Diarrhoea	7 (1.91%)	2 (0.54%)	9 (1.23%)
Vomiting	5 (1.37%)	0 (0.00%)	5 (0.68%)

Infections and infestations			
Conjunctivitis - Fellow Eye	4 (1.09%)	4 (1.09%)	8 (1.09%)
Conjunctivitis - Study Eye	5 (1.37%)	5 (1.36%)	10 (1.36%)
COVID-19	9 (2.46%)	16 (4.35%)	25 (3.41%)
Cystitis	3 (0.82%)	5 (1.36%)	8 (1.09%)
Hordeolum - Study Eye	4 (1.09%)	2 (0.54%)	6 (0.82%)
Nasopharyngitis	12 (3.28%)	11 (2.99%)	23 (3.13%)
Urinary tract infection	11 (3.01%)	10 (2.72%)	21 (2.86%)
Injury, poisoning and procedural complications			
Fall	6 (1.64%)	9 (2.45%)	15 (2.04%)
Intra-ocular injection complication - Study Eye	6 (1.64%)	3 (0.82%)	9 (1.23%)
Vaccination complication	3 (0.82%)	4 (1.09%)	7 (0.95%)
Investigations			
Gamma-glutamyltransferase increased	4 (1.09%)	3 (0.82%)	7 (0.95%)
Intraocular pressure increased - Study Eye	5 (1.37%)	10 (2.72%)	15 (2.04%)
Metabolism and nutrition disorders			
Diabetes mellitus	4 (1.09%)	1 (0.27%)	5 (0.68%)
Hypercholesterolaemia	4 (1.09%)	6 (1.63%)	10 (1.36%)
Hyperuricaemia	1 (0.27%)	4 (1.09%)	5 (0.68%)
Musculoskeletal and connective tissue disorders			
Back pain	8 (2.19%)	8 (2.17%)	16 (2.18%)
Osteoarthritis	6 (1.64%)	2 (0.54%)	8 (1.09%)
Nervous system disorders			

Carpal tunnel syndrome	4 (1.09%)	0 (0.00%)	4 (0.54%)
Dizziness	4 (1.09%)	2 (0.54%)	6 (0.82%)
Headache	10 (2.73%)	11 (2.99%)	21 (2.86%)
Psychiatric disorders			
Anxiety	5 (1.37%)	0 (0.00%)	5 (0.68%)
Respiratory, thoracic and mediastinal disorders			
Cough	4 (1.09%)	3 (0.82%)	7 (0.95%)
Vascular disorders			
Hypertension	18 (4.92%)	17 (4.62%)	35 (4.77%)

Other Relevant Findings

None

Conclusion:

Superiority of brolucizumab to aflibercept was established with the distribution of the last interval with no disease activity up to Week 32 (primary endpoint) as assessed with one-sided Wilcoxon test with type I error α = 0.025. The analysis results of the distribution of the last interval with no disease activity up to Week 64 (secondary endpoint) was robust and further supported the primary endpoint.

Non-inferiority of brolucizumab to aflibercept was established on visual acuity (change from baseline in best-corrected visual acuity (BCVA) at Week 32; primary endpoint), with a non-inferiority margin of 4 letters (p<0.001). The Week 64

results for change from baseline in BCVA (secondary endpoint) were consistent with the Week 32 results, favoring the brolucizumab to aflibercept.

Superiority of brolucizumab 6 mg compared with aflibercept 2 mg in terms of durability was established and non-inferiority of brolucizumab 6 mg to aflibercept 2 mg on visual acuity was demonstrated in this study (co-primary endpoints at Week 32). The safety profile of brolucizumab was consistent with the previously established profile of brolucizumab in the treatment of Neovascular age-related macular degeneration (nAMD) and no new safety signal or concern were identified.

Date of Clinical Trial Report

10 Aug 2023