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Trial record **1 of 1** for: CRFB002D2301

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A 12 Month Core Study to Assess the Efficacy and Safety of Ranibizumab (Intravitreal Injections) in Patients With Visual Impairment Due to Diabetic Macular Edema and a 24 Month Open-label Extension Study (RESTORE)

This study has been completed.

Sponsor:
Novartis

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT00687804

First received: May 27, 2008
Last updated: March 26, 2013
Last verified: March 2013
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Results First Received: January 19, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Diabetic Macular Edema
	Drug: Ranibizumab

Interventions:	Procedure: Laser Procedure: Sham laser Drug: Sham to ranibizumab

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
Participants who completed the 12 month randomized core study CRFB002D2301 were eligible to participate in the 24 month open-label extension study CRFB002D2301E1. The reporting groups for the participants in the extension study are according to their assigned treatment groups in the core study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could

	receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Participant Flow for 2 periods

Period 1: Core Study

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser
STARTED	**116**	**118**	**111**

COMPLETED	102	103	98
NOT COMPLETED	14	15	13
Adverse Event	5	3	3
Abnormal laboratory value(s)	1	0	0
Lack of Efficacy	1	1	1
Withdrawal by Subject	4	7	7
Lost to Follow-up	0	1	0
Death	2	2	2
Protocol Violation	1	1	0

Period 2: Open-Label Extension Study

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser
STARTED	83	83	74
Did Not Receive Ranibizumab in Extension	16	21	15
COMPLETED	73	72	63
NOT COMPLETED	10	11	11
Adverse Event	2	2	2
Subject withdrew consent	3	4	4
Lost to Follow-up	2	1	2
Administrative problems	1	1	0
Death	2	3	3

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Laser	Laser photocoagulation treatment was administered on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met:

	Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Total	Total of all reporting groups

Baseline Measures

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser	Total
Number of Participants [units: participants]	**116**	**118**	**111**	**345**
Age [units: years] Mean (Standard Deviation)	**62.9 (9.29)**	**64.0 (8.15)**	**63.5 (8.81)**	**63.5 (8.75)**
Age, Customized [units: Participants]				
< 55 years	**24**	**14**	**13**	**51**
55 - <65 years	**41**	**42**	**53**	**136**
65 - <75 years	**40**	**53**	**31**	**124**
>=75 years	**11**	**9**	**14**	**34**
Gender [units: participants]				
Female	**43**	**48**	**53**	**144**
Male	**73**	**70**	**58**	**201**

Outcome Measures

Hide All Outcome Measures

1. Primary: Core Study: Difference Between the Baseline Level of Visual Acuity (Letters) of the Study Eye and the Mean Visual Acuity Averaged Over All Monthly Post-baseline Assessments From Month 1 to Month 12 [Time Frame: Baseline through the end of study (Month 12)]

Measure Type	Primary
Measure Title	Core Study: Difference Between the Baseline Level of Visual Acuity (Letters) of the Study Eye and the Mean Visual Acuity Averaged Over All Monthly Post-baseline Assessments From Month 1 to Month 12
Measure Description	Visual acuity (VA) was assessed on both eyes during every study visit using best correction determined from protocol refraction. VA measurements (number of letters correctly identified) were performed with the patient in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS)-like visual acuity testing charts at a testing distance of 4 meters.
Time Frame	Baseline through the end of study (Month 12)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set consists of all patients who received at least one application of study treatment and had at least one post-baseline assessment for BCVA. Following the intent to treat principle, patients were analyzed according to the treatment assigned. Last Observation Carried Forward (LOCF) imputation was utilized.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits.

	Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Laser	Laser photocoagulation treatment was administered on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser
Number of Participants Analyzed [units: participants]	**115**	**118**	**110**
Core Study: Difference Between the Baseline Level of Visual Acuity (Letters) of the Study Eye and the			

Mean Visual Acuity Averaged Over All Monthly Post-baseline Assessments From Month 1 to Month 12 **[units: Letters]** **Mean (Standard Deviation)**			
Baseline	**64.7 (10.07)**	**63.4 (9.99)**	**62.6 (11.01)**
Average Month 1 to month 12	**70.8 (10.53)**	**69.2 (11.44)**	**63.4 (12.26)**
Change from Baseline	**6.1 (6.43)**	**5.9 (7.92)**	**0.8 (8.56)**

No statistical analysis provided for Core Study: Difference Between the Baseline Level of Visual Acuity (Letters) of the Study Eye and the Mean Visual Acuity Averaged Over All Monthly Post-baseline Assessments From Month 1 to Month 12

2. Primary: Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 24 Month Extension Study [Time Frame: Extension baseline (Month 12 -end of core study) to Month 36 (end of extension study) [24 Months]]

Measure Type	Primary
Measure Title	Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 24 Month Extension Study
Measure Description	Participants with ocular (occurring in the eye) serious adverse events (SAEs) and non-serious AEs in the study eye. The study eye is the eye that received the treatment. AEs are the appearance or worsening of any undesirable sign, symptom, or medical condition occurring after starting the study drug even if the event is not considered to be related to study drug. A serious adverse event is defined as an event that is fatal or life-threatening, results in persistent or significant disability/incapacity, constitutes a congenital anomaly/birth defect, requires inpatient hospitalization or prolongation of existing hospitalization or is medically significant. Additional information about adverse events can be found in the Adverse Event section.

Time Frame	Extension baseline (Month 12 -end of core study) to Month 36 (end of extension study) [24 Months]
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Safety Population included all participants who entered the extension and who had at least one safety assessment in the extension study. Participants were grouped according to the treatment assigned in the Core study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits.

	Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser With Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser Without Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser With Ranibizumab in Extension	Laser Without Ranibizumab in Extension
Number of Participants Analyzed [units: participants]	**83**	**83**	**59**	**15**
Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 24 Month Extension Study [units: Percentage of participants]				
Adverse Events	**56.6**	**56.6**	**52.5**	**40.0**
Serious Adverse Events	**2.4**	**1.2**	**1.7**	**0.0**

No statistical analysis provided for Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 24 Month Extension Study

3. Primary: Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 24 Month Extension Study [Time Frame: Extension baseline (Month 12 -end of core study) to Month 36 (end of extension study) [24 Months]]

Measure Type	Primary
Measure Title	Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 24 Month Extension Study
Measure Description	Participants with non-ocular (not occurring in the eye) serious adverse events (SAEs) and non-serious AEs. AEs are the appearance or worsening of of any undesirable sign, symptom, or medical condition occurring after starting the study drug even if the event is not considered to be related to study drug. A serious adverse event is defined as an event that is fatal or life-threatening, results in persistent or significant disability/incapacity, constitutes a congenital anomaly/birth defect, requires inpatient hospitalization or prolongation of existing hospitalization or is medically significant. Additional information about adverse events can be found in the Adverse Event section.

Time Frame	Extension baseline (Month 12 -end of core study) to Month 36 (end of extension study) [24 Months]
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Safety Population included all participants who entered the extension and who had at least one safety assessment in the extension study. Participants were grouped according to the treatment assigned in the Core study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits.

	Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser With Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser Without Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser With Ranibizumab in Extension	Laser Without Ranibizumab in Extension
Number of Participants Analyzed [units: participants]	**83**	**83**	**59**	**15**
Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 24 Month Extension Study [units: Percentage of participants]				
Adverse Events	**73.5**	**73.5**	**71.2**	**73.3**
Serious Adverse Events	**27.7**	**30.1**	**37.3**	**13.3**

No statistical analysis provided for Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 24 Month Extension Study

4. Secondary: Core Study: Categorized Change in Visual Acuity (Letters) of the Study Eye From Baseline at Month 12 [Time Frame: Baseline to Month 12]

Measure Type	Secondary
Measure Title	Core Study: Categorized Change in Visual Acuity (Letters) of the Study Eye From Baseline at Month 12
Measure Description	Visual acuity (VA) was assessed on both eyes during every study visit using best correction determined from protocol refraction. VA measurements (number of letters correctly identified) were performed with the patient in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS)-like visual acuity testing charts at a testing distance of 4 meters.
Time Frame	Baseline to Month 12
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set consists of all patients who received at least one application of study treatment and had at least one post-baseline assessment for BCVA. Following the intent to treat principle, patients were analyzed according to the treatment assigned. Last Observation Carried Forward (LOCF) imputation was utilized.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Laser	Laser photocoagulation treatment was administered on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in

	the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser
Number of Participants Analyzed [units: participants]	**115**	**118**	**110**
Core Study: Categorized Change in Visual Acuity (Letters) of the Study Eye From Baseline at Month 12 [units: Participants]			
Gain of ≥ 10 letters	**43**	**51**	**17**
Loss of ≥ 10 letters	**4**	**5**	**14**
Gain of ≥ 15 letters	**26**	**27**	**9**
Loss of ≥ 15 letters	**1**	**4**	**9**

No statistical analysis provided for Core Study: Categorized Change in Visual Acuity (Letters) of the Study Eye From Baseline at Month 12

5. Secondary: Core Study: Mean Change From Baseline in Visual Acuity (Letters) of the Study Eye Over Time [Time Frame: Baseline to Month 12]

Measure Type	Secondary
Measure Title	Core Study: Mean Change From Baseline in Visual Acuity (Letters) of the Study Eye Over Time
Measure Description	Visual acuity (VA) was assessed on both eyes during every study visit using best correction determined from protocol refraction. VA measurements (number of letters correctly identified) were performed with the patient in a sitting

	position using Early Treatment Diabetic Retinopathy Study (ETDRS)-like visual acuity testing charts at a testing distance of 4 meters.
Time Frame	Baseline to Month 12
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full analysis set, utilizing last observation carried forward.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.

Laser	Laser photocoagulation treatment was administered on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser
Number of Participants Analyzed [units: participants]	**115**	**118**	**110**
Core Study: Mean Change From Baseline in Visual Acuity (Letters) of the Study Eye Over Time [units: Letters] Mean (Standard Error)			
Month 1	**2.9 (0.49)**	**3.1 (0.56)**	**0.5 (0.64)**
Month 2	**4.4 (0.64)**	**4.9 (0.56)**	**0.4 (0.84)**
Month 3	**5.9 (0.65)**	**5.8 (0.65)**	**-0.5 (0.92)**
Month 4	**5.3 (0.68)**	**5.4 (0.69)**	**0.5 (0.92)**
Month 5	**5.9 (0.68)**	**5.7 (0.76)**	**0.9 (0.88)**
Month 6	**6.7 (0.68)**	**6.2 (0.78)**	**0.9**

			(0.94)
Month 7	**7.0 (0.72)**	**6.5 (0.84)**	**1.1 (0.98)**
Month 8	**7.1 (0.75)**	**6.4 (1.06)**	**1.3 (0.96)**
Month 9	**6.8 (0.76)**	**6.8 (1.05)**	**1.4 (0.90)**
Month 10	**7.3 (0.77)**	**6.4 (1.04)**	**0.8 (1.00)**
Month 11	**6.9 (0.79)**	**6.8 (1.10)**	**1.4 (0.95)**
Month 12	**6.8 (0.77)**	**6.4 (1.08)**	**0.9 (1.09)**

No statistical analysis provided for Core Study: Mean Change From Baseline in Visual Acuity (Letters) of the Study Eye Over Time

6. Secondary: Core Study: Mean Change From Baseline at Month 12 in Central Retinal Thickness of the Study Eye [Time Frame: Baseline to Month 12]

Measure Type	Secondary
Measure Title	Core Study: Mean Change From Baseline at Month 12 in Central Retinal Thickness of the Study Eye
Measure Description	Retinal thickness was measured using Optical Coherence Tomography (OCT). The images were reviewed by a central reading center to ensure a standardized evaluation.
Time Frame	Baseline to Month 12
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The number analyzed is the Full Analysis Set, including patients with a value at both baseline and the Month 12 visit. Last Observation Carried Forward imputation was utilized.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Laser	Laser photocoagulation treatment was administered on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed

	at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser
Number of Participants Analyzed [units: participants]	**113**	**116**	**108**
Core Study: Mean Change From Baseline at Month 12 in Central Retinal Thickness of the Study Eye [units: Micrometers] Mean (Standard Deviation)			
Baseline	**427.1 (118.42)**	**416.4 (119.91)**	**412.4 (124.53)**
Value at Month 12	**308.4 (112.26)**	**288.2 (90.11)**	**351.1 (139.91)**
Change from Baseline	**-118.7 (115.07)**	**-128.3 (114.34)**	**-61.3 (132.29)**

No statistical analysis provided for Core Study: Mean Change From Baseline at Month 12 in Central Retinal Thickness of the Study Eye

7. Secondary: Core Study: Mean Change From Baseline in Patient-reported Visual Functioning [Time Frame: Baseline to Month 12]

Measure Type	Secondary
Measure Title	Core Study: Mean Change From Baseline in Patient-reported Visual Functioning
Measure Description	The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) was used to measure a patient's subjective assessment of vision-related quality of life. The 12 subscales in the VFQ-25 are general health, general vision, ocular

	pain, near activities, distance activities, social function, mental health, role difficulties, dependency, driving, color vision, and peripheral vision. The scores on the subscales were added together for a total score, which ranged from 0 to 100. A higher score indicated improvement in quality of life due to vision function.
Time Frame	Baseline to Month 12
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The number analyzed is the Full Analysis Set, including the number of patients with a value at both baseline and the Month 12 visit. Last Observation Carried Forward imputation was utilized.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician.

	Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.
Laser	Laser photocoagulation treatment was administered on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser
Number of Participants Analyzed [units: participants]	**114**	**116**	**108**
Core Study: Mean Change From Baseline in Patient-reported Visual Functioning [units: Units on a scale] Mean (Standard Deviation)			
Baseline	**72.8 (16.91)**	**74.1 (18.06)**	**73.5 (18.18)**
Month 12	**77.8 (19.19)**	**79.5 (17.29)**	**74.1 (18.80)**
Change from Baseline	**5.0 (12.97)**	**5.4 (11.14)**	**0.6 (12.56)**

No statistical analysis provided for Core Study: Mean Change From Baseline in Patient-reported Visual Functioning

8. Secondary: Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 36 Months of the Core and Extension Studies [Time Frame: Core baseline (Day 1 of the core study) to Month 36 (end of extension study) [36 months]]

Measure Type	Secondary
Measure Title	Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 36 Months of the Core and Extension Studies
Measure Description	Participants with ocular (occurring in the eye) serious adverse events (SAEs) and non-serious AEs in the study eye. The study eye is the eye that received the treatment. AEs are the appearance or worsening of any undesirable sign, symptom, or medical condition occurring after starting the study drug even if the event is not considered to be related to study drug. A serious adverse event is defined as an event that is fatal or life-threatening, results in persistent or significant disability/incapacity, constitutes a congenital anomaly/birth defect, requires inpatient hospitalization or prolongation of existing hospitalization or is medically significant. Additional information about adverse events can be found in the Adverse Event section.
Time Frame	Core baseline (Day 1 of the core study) to Month 36 (end of extension study) [36 months]
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Safety Population included all participants who entered the extension and who had at least one safety assessment in the extension study. Participants were grouped according to the treatment assigned in the Core study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last

	2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser With Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab

	0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser Without Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser With Ranibizumab in Extension	Laser Without Ranibizumab in Extension
Number of Participants Analyzed [units: participants]	**83**	**83**	**59**	**15**
Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 36 Months of the Core and Extension Studies [units: Percentage of participants]				
Adverse Events	**66.3**	**67.5**	**64.4**	**46.7**
Serious Adverse Events	**2.4**	**3.6**	**5.1**	**0.0**

No statistical analysis provided for Extension Study: Percentage of Participants With Ocular Adverse Events (AEs) in the Study Eye in the 36 Months of the Core and Extension Studies

9. Secondary: Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 36 Months of the Core and Extension Studies [Time Frame: Core baseline (Day 1 of the core study) to Month 36 (end of extension study) [36 Months]]

Measure Type	Secondary
Measure Title	Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 36 Months of the Core and Extension Studies
Measure Description	Participants with non-ocular (not occurring in the eye) serious adverse events (SAEs) and non-serious AEs. AEs are the appearance or worsening of of any undesirable sign, symptom, or medical condition occurring after starting the study drug even if the event is not considered to be related to study drug. A serious adverse event is defined as an event that is fatal or life-threatening, results in persistent or significant disability/incapacity, constitutes a congenital anomaly/birth defect, requires inpatient hospitalization or prolongation of existing hospitalization or is medically significant. Additional information about Adverse Events can be found in the Adverse Event section.
Time Frame	Core baseline (Day 1 of the core study) to Month 36 (end of extension study) [36 Months]
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Safety Population included all participants who entered the extension and who had at least one safety assessment in the extension study. Participants were grouped according to the treatment assigned in the Core study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met:

	Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser With Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes.

	In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser Without Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser With Ranibizumab in Extension	Laser Without Ranibizumab in Extension
Number of Participants Analyzed [units: participants]	**83**	**83**	**59**	**15**
Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 36 Months of the Core and Extension Studies [units: Percentage of participants]				
Adverse Events	**83.1**	**81.9**	**84.7**	**73.3**
Serious Adverse Events	**36.1**	**37.3**	**42.4**	**13.3**

No statistical analysis provided for Extension Study: Percentage of Participants With Non-Ocular Adverse Events (AEs) in the 36 Months of the Core

and Extension Studies

10. Secondary: Extension Study: Mean Change From Extension Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36 [Time Frame: Extension baseline (Month12 -end of core study), Month 36 (end of extension study)]

Measure Type	Secondary
Measure Title	Extension Study: Mean Change From Extension Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36
Measure Description	Visual acuity (VA) was assessed on both eyes during every study visit using best correction determined from protocol refraction. VA measurements (number of letters correctly identified) were performed with the patient in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS)-like visual acuity testing charts at a testing distance of 4 meters. An increase in the number of letters read correctly indicates improvement.
Time Frame	Extension baseline (Month12 -end of core study), Month 36 (end of extension study)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants from the Safety Population that included all participants who entered the extension and who had at least one safety assessment in the extension study with data available for analyses. Participants were grouped according to the treatment assigned in the Core study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if

	deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Active Laser	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Active Laser
Number of Participants Analyzed [units: participants]	**83**	**80**	**74**
Extension Study: Mean Change From Extension Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36 [units: Letters] Mean (Standard Deviation)	**0.1 (9.10)**	**-0.5 (9.19)**	**3.7 (6.88)**

No statistical analysis provided for Extension Study: Mean Change From Extension Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36

11. Secondary: Extension Study: Mean Change From Core Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36 [Time Frame: Core baseline (Day 1 of the core study), Month 36 (end of extension study)]

Measure Type	Secondary
Measure Title	Extension Study: Mean Change From Core Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36
Measure Description	Visual acuity (VA) was assessed on both eyes during every study visit using best correction determined from protocol refraction. VA measurements (number of letters correctly identified) were performed with the patient in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS)-like visual acuity testing charts at a testing distance of 4 meters. An increase in the number of letters read correctly indicates improvement.
Time Frame	Core baseline (Day 1 of the core study), Month 36 (end of extension study)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Safety Population included all participants who entered the extension and who had at least one safety assessment in the extension study. Participants were grouped according to the treatment assigned in the Core study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Active Laser	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in

	the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Measured Values

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Active Laser
Number of Participants Analyzed [units: participants]	**83**	**83**	**74**
Extension Study: Mean Change From Core Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36 [units: Letters] Mean (Standard Deviation)	**8.0 (10.09)**	**6.7 (9.59)**	**6.0 (9.35)**

No statistical analysis provided for Extension Study: Mean Change From Core Study Baseline in Best Corrected Visual Acuity (BCVA) at Month 36

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	Safety Population included all randomized treated participants. Participants are grouped according to the treatment actually received in the Core Study.

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy
Laser With Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham

	intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Laser Without Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Serious Adverse Events

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser With Ranibizumab in Extension	Laser Without Ranibizumab in Extension
Total, serious adverse events				
# participants affected / at risk	**41/115 (35.65%)**	**43/120 (35.83%)**	**28/59 (47.46%)**	**7/51 (13.73%)**

Blood and lymphatic system disorders				
Anaemia † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**1/120 (0.83%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Febrile neutropenia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Hypochromic anaemia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Lymphadenopathy † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Spleen disorder † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Splenic infarction † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Cardiac disorders				
Acute myocardial infarction † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**2/59 (3.39%)**	**0/51 (0.00%)**
Angina pectoris † [1]				
# participants affected / at risk	**3/115 (2.61%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Angina unstable † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Aortic valve stenosis † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Arrhythmia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Atrial fibrillation † [1]				

# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Cardiac disorder † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	0/59 (0.00%)	1/51 (1.96%)
Cardiac failure † [1]				
# participants affected / at risk	1/115 (0.87%)	1/120 (0.83%)	4/59 (6.78%)	1/51 (1.96%)
Cardiac failure congestive † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Cardiogenic shock † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Cardiopulmonary failure † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Coronary artery disease † [1]				
# participants affected / at risk	3/115 (2.61%)	1/120 (0.83%)	1/59 (1.69%)	0/51 (0.00%)
Coronary artery occlusion † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Mitral valve incompetence † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Myocardial infarction † [1]				
# participants affected / at risk	1/115 (0.87%)	4/120 (3.33%)	3/59 (5.08%)	0/51 (0.00%)
Myocardial ischaemia † [1]				
# participants affected / at risk	1/115 (0.87%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Right ventricular failure † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Tachyarrhythmia † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Congenital, familial and genetic disorders				

Spinocerebellar ataxia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Ear and labyrinth disorders				
Deafness † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Vertigo † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Eye disorders				
Cataract (Fellow eye) † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**1/120 (0.83%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Cataract (Study eye) † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**3/120 (2.50%)**	**2/59 (3.39%)**	**0/51 (0.00%)**
Cataract subcapsular (Fellow eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Conjunctival haemorrhage (Study eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Corneal oedema (Study eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Diabetic retinal oedema (Fellow eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**1/120 (0.83%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Lenticular opacities (Study eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Vitreous adhesions (Study eye) † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**

Vitreous haemorrhage (Fellow eye) † [1]				
# participants affected / at risk	2/115 (1.74%)	0/120 (0.00%)	1/59 (1.69%)	1/51 (1.96%)
Vitreous haemorrhage (Study eye) † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Gastrointestinal disorders				
Abdominal hernia † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Abdominal pain † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Abdominal pain upper † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Colonic polyp † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Constipation † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Diarrhoea † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	1/59 (1.69%)	0/51 (0.00%)
Gastric haemorrhage † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	0/59 (0.00%)	1/51 (1.96%)
Gastric ulcer † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	0/59 (0.00%)	1/51 (1.96%)
Gastrointestinal necrosis † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Gastrointestinal obstruction † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)

Hernial eventration † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Intestinal obstruction † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Nausea † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Oesophagitis † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Pancreatitis acute † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**1/51 (1.96%)**
Subileus † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Umbilical hernia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Vomiting † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
General disorders				
Chest discomfort † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Malaise † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Multi-organ failure † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Oedema peripheral † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**

Polyserositis † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Pyrexia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Hepatobiliary disorders				
Bile duct obstruction † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Cholecystitis † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Cholelithiasis † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Hepatic function abnormal † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Infections and infestations				
Appendicitis † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Biliary sepsis † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Bronchitis † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Cellulitis † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Cholecystitis infective † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Gas gangrene † [1]				

# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Gastroenteritis † [1]				
# participants affected / at risk	1/115 (0.87%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Gastroenteritis norovirus † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Infection † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Localised infection † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Lower respiratory tract infection † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Mediastinitis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Osteomyelitis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Otitis media † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Pneumonia † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	3/59 (5.08%)	0/51 (0.00%)
Pneumonia cytomegaloviral † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Pseudomonas infection † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Sepsis † [1]				
# participants affected / at risk	1/115 (0.87%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)

Soft tissue infection † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Staphylococcal infection † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Systemic candida † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Urinary tract infection † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Injury, poisoning and procedural complications				
Back injury † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Contusion † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Coronary artery restenosis † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Eye injury (Fellow eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Eye injury (Study eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Eyelid injury (Study eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Fall † [1]				
# participants affected / at risk	**3/115 (2.61%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Femoral neck fracture † [1]				

# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Femur fracture † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Head injury † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Lower limb fracture † [1]				
# participants affected / at risk	1/115 (0.87%)	2/120 (1.67%)	0/59 (0.00%)	0/51 (0.00%)
Lumbar vertebral fracture † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Meniscus lesion † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Open wound † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Periorbital haematoma (Study eye) † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Post procedural complication † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Radius fracture † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Road traffic accident † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Spinal cord injury † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Tendon rupture † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Investigations				

Blood calcium increased † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Blood glucose increased † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Blood urea increased † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Body temperature decreased † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Metabolism and nutrition disorders				
Dehydration † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Diabetes mellitus † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**2/120 (1.67%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Diabetic foot † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**0/120 (0.00%)**	**3/59 (5.08%)**	**1/51 (1.96%)**
Hyperglycaemia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Hyperkalaemia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Hyperuricaemia † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Hypoglycaemia † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Obesity † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**

Type 2 diabetes mellitus † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Musculoskeletal and connective tissue disorders				
Intervertebral disc protrusion † [1]				
# participants affected / at risk	0/115 (0.00%)	3/120 (2.50%)	1/59 (1.69%)	0/51 (0.00%)
Lumbar spinal stenosis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Osteoarthritis † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Osteochondrosis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Spinal column stenosis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Spinal osteoarthritis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Spondylolisthesis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Colon cancer † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Gastric cancer † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Hepatic neoplasm † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)

Malignant neoplasm of ampulla of Vater † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Multiple myeloma † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Pancreatic carcinoma † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Prostate cancer † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Rectal cancer † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Renal cancer † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Urethral neoplasm † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Uterine leiomyoma † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Nervous system disorders				
Carotid artery stenosis † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	1/51 (1.96%)
Cerebral artery embolism † [1]				
# participants affected / at risk	1/115 (0.87%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Cerebrovascular accident † [1]				
# participants affected / at risk	3/115 (2.61%)	1/120 (0.83%)	1/59 (1.69%)	0/51 (0.00%)
Cerebrovascular disorder † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)

Diabetic neuropathy † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Dizziness † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Embolic stroke † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Hepatic encephalopathy † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Loss of consciousness † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Subarachnoid haemorrhage † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Syncope † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Transient ischaemic attack † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Psychiatric disorders				
Depression † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Renal and urinary disorders				
Acute prerenal failure † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Bladder prolapse † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Calculus urinary † [1]				

# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Nephrolithiasis † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Polyuria † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Renal colic † [1]				
# participants affected / at risk	0/115 (0.00%)	0/120 (0.00%)	1/59 (1.69%)	0/51 (0.00%)
Renal failure † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Renal failure acute † [1]				
# participants affected / at risk	1/115 (0.87%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Renal failure chronic † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	1/51 (1.96%)
Reproductive system and breast disorders				
Benign prostatic hyperplasia † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Respiratory, thoracic and mediastinal disorders				
Dyspnoea † [1]				
# participants affected / at risk	1/115 (0.87%)	1/120 (0.83%)	1/59 (1.69%)	0/51 (0.00%)
Epistaxis † [1]				
# participants affected / at risk	2/115 (1.74%)	0/120 (0.00%)	0/59 (0.00%)	0/51 (0.00%)
Nasal septum deviation † [1]				
# participants affected / at risk	0/115 (0.00%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)
Pulmonary embolism † [1]				
# participants affected / at risk	2/115 (1.74%)	1/120 (0.83%)	0/59 (0.00%)	0/51 (0.00%)

Pulmonary haematoma † 1				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Pulmonary oedema † 1				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Respiratory arrest † 1				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Sleep apnoea syndrome † 1				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**1/51 (1.96%)**
Skin and subcutaneous tissue disorders				
Acute febrile neutrophilic dermatosis † 1				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Dermatitis † 1				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Skin hypertrophy † 1				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Skin ulcer † 1				
# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Vascular disorders				
Arterial thrombosis limb † 1				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Deep vein thrombosis † 1				
# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Hypertension † 1				
# participants affected / at risk	**1/115 (0.87%)**	**2/120 (1.67%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Hypertensive crisis † 1				

# participants affected / at risk	**0/115 (0.00%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Hypotension † 1				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Peripheral arterial occlusive disease † 1				
# participants affected / at risk	**1/115 (0.87%)**	**1/120 (0.83%)**	**1/59 (1.69%)**	**0/51 (0.00%)**
Varicose vein † 1				
# participants affected / at risk	**1/115 (0.87%)**	**0/120 (0.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	Safety Population included all randomized treated participants. Participants are grouped according to the treatment actually received in the Core Study.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Ranibizumab 0.5 mg	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of

	20/20) was observed at the last 2 last visits. Patients also received sham laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.
Ranibizumab 0.5 mg + Laser	Ranibizumab 0.5 mg was administered monthly by intravitreal injection in the study eye for 3 months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Patients also received active laser treatment on Day 1 and subsequently at intervals of at least 3 months, if deemed necessary by the evaluating physician. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy
Laser With Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24

	injections) and could receive laser therapy.
Laser Without Ranibizumab in Extension	Active laser photocoagulation treatment was administered on Day 1 and at intervals of at least 3 months, if deemed necessary by the evaluating physician. Patients also received monthly sham intravitreal injection in the study eye for 3 consecutive months. After the third injection, treatment was suspended if either one of the following criteria was met: Improvement in best corrected visual acuity (BCVA) could not be attributed to treatment at the last 2 visits, in the opinion of the investigator, or BCVA > 84 letters (approximate Snellen equivalent of 20/20) was observed at the last 2 last visits. Active/sham laser treatment was always administered before (sham) intravitreal injections. The minimum interval between the 2 treatments was 30 minutes. In the extension study at the investigator's discretion, patients received open-label ranibizumab 0.5 mg intravitreal injections once a month until stable vision was reached (a maximum of 24 injections) and could receive laser therapy.

Other Adverse Events

	Ranibizumab 0.5 mg	Ranibizumab 0.5 mg + Laser	Laser With Ranibizumab in Extension	Laser Without Ranibizumab in Extension
Total, other (not including serious) adverse events				
# participants affected / at risk	**79/115 (68.70%)**	**83/120 (69.17%)**	**50/59 (84.75%)**	**31/51 (60.78%)**
Blood and lymphatic system disorders				
Anaemia † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**6/120 (5.00%)**	**3/59 (5.08%)**	**1/51 (1.96%)**
Eye disorders				
Blepharitis (Fellow eye) † [1]				

# participants affected / at risk	1/115 (0.87%)	1/120 (0.83%)	3/59 (5.08%)	1/51 (1.96%)
Cataract (Fellow eye) † [1]				
# participants affected / at risk	10/115 (8.70%)	12/120 (10.00%)	7/59 (11.86%)	5/51 (9.80%)
Cataract (Study eye) † [1]				
# participants affected / at risk	9/115 (7.83%)	17/120 (14.17%)	9/59 (15.25%)	4/51 (7.84%)
Conjunctival haemorrhage (Study eye) † [1]				
# participants affected / at risk	9/115 (7.83%)	13/120 (10.83%)	0/59 (0.00%)	0/51 (0.00%)
Conjunctival hyperaemia (Study eye) † [1]				
# participants affected / at risk	9/115 (7.83%)	8/120 (6.67%)	5/59 (8.47%)	2/51 (3.92%)
Conjunctivitis (Fellow eye) † [1]				
# participants affected / at risk	4/115 (3.48%)	6/120 (5.00%)	3/59 (5.08%)	1/51 (1.96%)
Diabetic retinal oedema (Fellow eye) † [1]				
# participants affected / at risk	12/115 (10.43%)	19/120 (15.83%)	11/59 (18.64%)	3/51 (5.88%)
Diabetic retinal oedema (Study eye) † [1]				
# participants affected / at risk	7/115 (6.09%)	6/120 (5.00%)	3/59 (5.08%)	1/51 (1.96%)
Diabetic retinopathy (Fellow eye) † [1]				
# participants affected / at risk	4/115 (3.48%)	6/120 (5.00%)	4/59 (6.78%)	2/51 (3.92%)

Diabetic retinopathy (Study eye) † [1]				
# participants affected / at risk	**3/115 (2.61%)**	**8/120 (6.67%)**	**3/59 (5.08%)**	**2/51 (3.92%)**
Dry eye (Fellow eye) † [1]				
# participants affected / at risk	**5/115 (4.35%)**	**4/120 (3.33%)**	**3/59 (5.08%)**	**3/51 (5.88%)**
Dry eye (Study eye) † [1]				
# participants affected / at risk	**5/115 (4.35%)**	**4/120 (3.33%)**	**3/59 (5.08%)**	**3/51 (5.88%)**
Eye discharge (Study eye) † [1]				
# participants affected / at risk	**4/115 (3.48%)**	**6/120 (5.00%)**	**1/59 (1.69%)**	**1/51 (1.96%)**
Eye haemorrhage (Fellow eye) † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**3/120 (2.50%)**	**3/59 (5.08%)**	**0/51 (0.00%)**
Eye haemorrhage (Study eye) † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**3/120 (2.50%)**	**3/59 (5.08%)**	**0/51 (0.00%)**
Eye irritation (Study eye) † [1]				
# participants affected / at risk	**3/115 (2.61%)**	**2/120 (1.67%)**	**3/59 (5.08%)**	**0/51 (0.00%)**
Eye pain (Study eye) † [1]				
# participants affected / at risk	**15/115 (13.04%)**	**11/120 (9.17%)**	**13/59 (22.03%)**	**2/51 (3.92%)**
Eye pruritus (Study eye) † [1]				
# participants affected / at risk	**3/115 (2.61%)**	**3/120 (2.50%)**	**5/59 (8.47%)**	**1/51 (1.96%)**
Foreign body sensation in eyes				

(Study eye) † [1]				
# participants affected / at risk	**5/115 (4.35%)**	**8/120 (6.67%)**	**2/59 (3.39%)**	**0/51 (0.00%)**
Lacrimation increased (Study eye) † [1]				
# participants affected / at risk	**3/115 (2.61%)**	**6/120 (5.00%)**	**5/59 (8.47%)**	**0/51 (0.00%)**
Macular fibrosis (Study eye) † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**2/120 (1.67%)**	**5/59 (8.47%)**	**0/51 (0.00%)**
Punctate keratitis (Fellow eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**6/120 (5.00%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Retinal aneurysm (Study eye) † [1]				
# participants affected / at risk	**0/115 (0.00%)**	**3/120 (2.50%)**	**3/59 (5.08%)**	**1/51 (1.96%)**
Retinal exudates (Fellow eye) † [1]				
# participants affected / at risk	**7/115 (6.09%)**	**3/120 (2.50%)**	**3/59 (5.08%)**	**1/51 (1.96%)**
Retinal exudates (Study eye) † [1]				
# participants affected / at risk	**4/115 (3.48%)**	**2/120 (1.67%)**	**5/59 (8.47%)**	**1/51 (1.96%)**
Retinal haemorrhage (Fellow eye) † [1]				
# participants affected / at risk	**4/115 (3.48%)**	**8/120 (6.67%)**	**2/59 (3.39%)**	**0/51 (0.00%)**
Vision blurred (Study eye) † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**4/120 (3.33%)**	**3/59 (5.08%)**	**2/51 (3.92%)**

Visual acuity reduced (Fellow eye) † [1]				
# participants affected / at risk	**4/115 (3.48%)**	**3/120 (2.50%)**	**3/59 (5.08%)**	**2/51 (3.92%)**
Visual acuity reduced (Study eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**2/120 (1.67%)**	**1/59 (1.69%)**	**3/51 (5.88%)**
Vitreous haemorrhage (Study eye) † [1]				
# participants affected / at risk	**1/115 (0.87%)**	**1/120 (0.83%)**	**3/59 (5.08%)**	**0/51 (0.00%)**
Gastrointestinal disorders				
Gastrooesophageal reflux disease † [1]				
# participants affected / at risk	**3/115 (2.61%)**	**0/120 (0.00%)**	**3/59 (5.08%)**	**0/51 (0.00%)**
Nausea † [1]				
# participants affected / at risk	**6/115 (5.22%)**	**5/120 (4.17%)**	**2/59 (3.39%)**	**3/51 (5.88%)**
Vomiting † [1]				
# participants affected / at risk	**2/115 (1.74%)**	**1/120 (0.83%)**	**2/59 (3.39%)**	**3/51 (5.88%)**
Infections and infestations				
Bronchitis † [1]				
# participants affected / at risk	**6/115 (5.22%)**	**4/120 (3.33%)**	**1/59 (1.69%)**	**2/51 (3.92%)**
Influenza † [1]				
# participants affected / at risk	**12/115 (10.43%)**	**8/120 (6.67%)**	**8/59 (13.56%)**	**5/51 (9.80%)**

Nasopharyngitis † [1]				
# participants affected / at risk	18/115 (15.65%)	21/120 (17.50%)	15/59 (25.42%)	8/51 (15.69%)
Pneumonia † [1]				
# participants affected / at risk	2/115 (1.74%)	2/120 (1.67%)	0/59 (0.00%)	3/51 (5.88%)
Injury, poisoning and procedural complications				
Fall † [1]				
# participants affected / at risk	4/115 (3.48%)	5/120 (4.17%)	4/59 (6.78%)	1/51 (1.96%)
Investigations				
Blood glucose increased † [1]				
# participants affected / at risk	1/115 (0.87%)	3/120 (2.50%)	3/59 (5.08%)	1/51 (1.96%)
Intraocular pressure increased (Fellow eye) † [1]				
# participants affected / at risk	3/115 (2.61%)	6/120 (5.00%)	0/59 (0.00%)	1/51 (1.96%)
Musculoskeletal and connective tissue disorders				
Arthralgia † [1]				
# participants affected / at risk	6/115 (5.22%)	1/120 (0.83%)	3/59 (5.08%)	0/51 (0.00%)
Back pain † [1]				
# participants affected / at risk	7/115 (6.09%)	5/120 (4.17%)	8/59 (13.56%)	1/51 (1.96%)
Muscle spasms † [1]				

# participants affected / at risk	**0/115 (0.00%)**	**1/120 (0.83%)**	**4/59 (6.78%)**	**0/51 (0.00%)**
Pain in extremity † 1				
# participants affected / at risk	**6/115 (5.22%)**	**1/120 (0.83%)**	**0/59 (0.00%)**	**0/51 (0.00%)**
Nervous system disorders				
Dizziness † 1				
# participants affected / at risk	**2/115 (1.74%)**	**2/120 (1.67%)**	**3/59 (5.08%)**	**1/51 (1.96%)**
Headache † 1				
# participants affected / at risk	**4/115 (3.48%)**	**5/120 (4.17%)**	**5/59 (8.47%)**	**1/51 (1.96%)**
Renal and urinary disorders				
Renal failure † 1				
# participants affected / at risk	**1/115 (0.87%)**	**2/120 (1.67%)**	**4/59 (6.78%)**	**1/51 (1.96%)**
Respiratory, thoracic and mediastinal disorders				
Cough † 1				
# participants affected / at risk	**3/115 (2.61%)**	**4/120 (3.33%)**	**4/59 (6.78%)**	**1/51 (1.96%)**
Vascular disorders				
Hypertension † 1				
# participants affected / at risk	**15/115 (13.04%)**	**11/120 (9.17%)**	**6/59 (10.17%)**	**6/51 (11.76%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. ☑ **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862 778-8300

No publications provided by Novartis

Publications automatically indexed to this study:

Mitchell P, Massin P, Bressler S, Coon CD, Petrillo J, Ferreira A, Bressler NM. Three-year patient-reported visual function outcomes in diabetic macular edema managed with ranibizumab: the RESTORE extension study. Curr Med Res Opin. 2015 Nov;31(11):1967-75. doi: 10.1185/03007995.2015.1081880. Epub 2015 Oct 6.

Bressler NM, Varma R, Suñer IJ, Dolan CM, Ward J, Ehrlich JS, Colman S, Turpcu A; RIDE and RISE Research Groups. Vision-related function after ranibizumab treatment for diabetic macular edema: results from RIDE and RISE. Ophthalmology. 2014 Dec;121(12):2461-72. doi: 10.1016/j.ophtha.2014.07.008. Epub 2014 Aug 20.

Mitchell P, Bressler N, Tolley K, Gallagher M, Petrillo J, Ferreira A, Wood R, Bandello F; RESTORE Study Group. Patient-reported visual function outcomes improve after ranibizumab treatment in patients with vision impairment due to diabetic macular edema: randomized clinical trial. JAMA Ophthalmol. 2013 Oct;131(10):1339-47. doi: 10.1001/jamaophthalmol.2013.4592.

Mitchell P, Bandello F, Schmidt-Erfurth U, Lang GE, Massin P, Schlingemann RO, Sutter F, Simader C, Burian G, Gerstner O, Weichselberger A; RESTORE study group. The RESTORE study: ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. Ophthalmology. 2011 Apr;118(4):615-25. doi: 10.1016/j.ophtha.2011.01.031.

Schmidt-Erfurth U, Lang GE, Holz FG, Schlingemann RO, Lanzetta P, Massin P, Gerstner O, Bouazza AS, Shen H, Osborne A, Mitchell P; RESTORE Extension Study Group. Three-year outcomes of individualized ranibizumab treatment in patients with diabetic macular edema: the RESTORE extension study. Ophthalmology. 2014 May;121(5):1045-53. doi: 10.1016/j.ophtha.2013.11.041. Epub 2014 Feb 1.

Responsible Party:	Novartis
ClinicalTrials.gov Identifier:	NCT00687804 History of Changes
Obsolete Identifiers:	NCT00906464
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Health Authority:	Switzerland: Swissmedic

Australia: Department of Health and Ageing Therapeutic Goods Administration
Belgium: Federal Agency for Medicinal Products and Health Products
Germany: Paul-Ehrlich-Institut
Spain: Spanish Agency of Medicines
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Greece: National Organization of Medicines
Hungary: National Institute of Pharmacy
Netherlands: The Central Committee on Research Involving Human Subjects (CCMO)
United Kingdom: Medicines and Healthcare Products Regulatory Agency