Safety and Efficacy of Ranibizumab in Diabetic Macular Edema (RELATION)

This study has been terminated.
(European drug approval.)

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT01131585

First received: May 25, 2010
Last updated: August 20, 2012
Last verified: August 2012
History of Changes

Results First Received: July 12, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Visual Impairment Due to Diabetic Macular Edema
Interventions:	Procedure: Active laser photocoagulation Drug: Sham injections Drug: Ranibizumab 0.5 mg

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
Participants did not complete study due to early termination. Study was terminated because of drug approval.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Active Laser Photocoagulation and Ranibizumab	Active laser treatment applied at baseline and reapplied if needed at intervals no shorter than 3 months from the last treatment. Ranibizumab intravitreal injection given at baseline, 30, 60 and 90 days and if needed, reapplied at intervals no shorter than 28 days from last treatment.
Active Laser Photocoagulation and Sham Injection	Active laser treatment applied at baseline and reapplied if needed at intervals no shorter than 3 months from the last treatment.

	Sham intravitreal injection given at baseline, 30, 60 and 90 days and if needed, reapplied at intervals no shorter than 28 days from last treatment.

Participant Flow: Overall Study

	Active Laser Photocoagulation and Ranibizumab	Active Laser Photocoagulation and Sham Injection
STARTED	**85**	**43**
COMPLETED	**0**	**0**
NOT COMPLETED	**85**	**43**
Adverse Event	**0**	**2**
Abnormal laboratory value	**1**	**0**
Unsatisfactory therapeutic effect	**0**	**3**
Protocol Violation	**2**	**1**
Withdrawal by Subject	**3**	**3**
Lost to Follow-up	**0**	**1**
Administrative problems	**1**	**1**
Study termination	**78**	**32**

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

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Total	Total of all reporting groups

Baseline Measures

	Active Laser Photocoagulation and Ranibizumab	Active Laser Photocoagulation and Sham Injection	Total
Number of Participants [units: participants]	**85**	**43**	**128**
Age [units: years]			

Mean (Standard Deviation)			
>=18 years	**63.5 (9.3)**	**63.5 (10.5)**	**63.5 (9.7)**
Gender [units: participants]			
Female	**32**	**16**	**48**
Male	**53**	**27**	**80**

Outcome Measures

1. Primary: Change in Best-Corrected Visual Acuity (BCVA) From Baseline to Month 12 [Time Frame: 12 months]

Hide Outcome Measure 1

Measure Type	Primary
Measure Title	Change in Best-Corrected Visual Acuity (BCVA) From Baseline to Month 12
Measure Description	Mean change in Best-Corrected Visual Acuity (BCVA) letters at 12 months compared to baseline was measured using Visual acuity (VA). VA accounts for the number of letters a participant can see using Early Treatment Diabetic Retinopathy Study (EDTRS)-like visual acuity testing charts, from a sitting position at a testing distance of 4 meters. BCVA means that the participant's refraction is already taken into account when VA is determined. A higher BCVA number at 12 months in reference to baseline indicates improved BCVA.
Time Frame	12 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.
Full Analysis Set consisted of all participants who received at least one application of study treatment and had at least one post-baseline assessment for BCVA. No patient completed the 12 months observational period due to study early termination; therefore, the last observation carried forward (LOCF) method was used with data from 11.1 months.

Reporting Groups

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Measured Values

	Active Laser Photocoagulation and Ranibizumab	**Active Laser Photocoagulation and Sham Injection**
Number of Participants Analyzed [units: participants]	**85**	**43**
Change in Best-Corrected Visual Acuity (BCVA) From Baseline to Month 12	**6.5 (8.6)**	**1.4 (7.3)**

[units: Letters] **Mean (Standard Deviation)**		

No statistical analysis provided for Change in Best-Corrected Visual Acuity (BCVA) From Baseline to Month 12

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

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Serious Adverse Events

	Active Laser Photocoagulation and Ranibizumab	Active Laser Photocoagulation and Sham Injection
Total, serious adverse events		
# participants affected / at risk	**14/85 (16.47%)**	**5/43 (11.63%)**
Cardiac disorders		
CARDIAC FAILURE CONGESTIVE † 1		
# participants affected / at risk	**1/85 (1.18%)**	**0/43 (0.00%)**
CORONARY ARTERY DISEASE † 1		
# participants affected / at risk	**0/85 (0.00%)**	**1/43 (2.33%)**
CORONARY ARTERY STENOSIS † 1		
# participants affected / at risk	**0/85 (0.00%)**	**1/43 (2.33%)**
Eye disorders		
DIABETIC RETINAL OEDEMA (Study eye) † 1		
# participants affected / at risk	**1/85 (1.18%)**	**0/43 (0.00%)**
DIABETIC RETINOPATHY (Fellow eye) † 1		
# participants affected / at risk	**1/85 (1.18%)**	**0/43 (0.00%)**
RETINAL DETACHMENT (Fellow eye) † 1		
# participants affected / at risk	**0/85 (0.00%)**	**2/43 (4.65%)**
VITREOUS HAEMORRHAGE (Fellow eye) † 1		
# participants affected / at risk	**0/85 (0.00%)**	**1/43 (2.33%)**
Gastrointestinal disorders		
ANAL SPHINCTER ATONY † 1		

# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
General disorders		
CONCOMITANT DISEASE PROGRESSION † 1		
# participants affected / at risk	0/85 (0.00%)	1/43 (2.33%)
Hepatobiliary disorders		
CHOLECYSTITIS † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
Infections and infestations		
CELLULITIS † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
PNEUMONIA † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
Metabolism and nutrition disorders		
DIABETES MELLITUS † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
DIABETIC FOOT † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
HYPOGLYCAEMIA † 1		
# participants affected / at risk	2/85 (2.35%)	0/43 (0.00%)
TYPE 1 DIABETES MELLITUS † 1		
# participants affected / at risk	0/85 (0.00%)	1/43 (2.33%)
Musculoskeletal and connective tissue disorders		
CHONDROPATHY † 1		
# participants affected / at risk	0/85 (0.00%)	1/43 (2.33%)
OSTEOARTHRITIS † 1		
# participants affected / at risk	0/85 (0.00%)	1/43 (2.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
GASTROINTESTINAL TRACT ADENOMA † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
Nervous system disorders		
CEREBROVASCULAR ACCIDENT † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
LOSS OF CONSCIOUSNESS † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
Vascular disorders		
HYPERTENSION † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
HYPERTENSIVE CRISIS † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)
THROMBOPHLEBITIS † 1		
# participants affected / at risk	1/85 (1.18%)	0/43 (0.00%)

† Events were collected by systematic assessment
1 Term from vocabulary, 14.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5

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Other Adverse Events

	Active Laser Photocoagulation and Ranibizumab	Active Laser Photocoagulation and Sham Injection
Total, other (not including serious) adverse events		
# participants affected / at risk	**32/85 (37.65%)**	**10/43 (23.26%)**
Eye disorders		
EYE IRRITATION (Study eye) † 1		
# participants affected / at risk	**5/85 (5.88%)**	**0/43 (0.00%)**
# events	**5**	**0**
EYE PAIN (Study eye) † 1		
# participants affected / at risk	**13/85 (15.29%)**	**4/43 (9.30%)**
# events	**13**	**4**
LACRIMATION INCREASED (Study eye) † 1		
# participants affected / at risk	**5/85 (5.88%)**	**1/43 (2.33%)**
# events	**5**	**1**
Infections and infestations		
NASOPHARYNGITIS † 1		
# participants affected / at risk	**13/85 (15.29%)**	**6/43 (13.95%)**
# events	**13**	**6**
Nervous system disorders		
HEADACHE † 1		
# participants affected / at risk	**5/85 (5.88%)**	**1/43 (2.33%)**
# events	**5**	**1**

Vascular disorders		
HYPERTENSION † 1		
# participants affected / at risk	**4/85 (4.71%)**	**4/43 (9.30%)**
# events	**4**	**4**

† Events were collected by systematic assessment
1 Term from vocabulary, 14.0

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
Early study termination due to European drug approval.

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 or disclosure of trial results in their entirety.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 41 61 324 1111

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT01131585 History of Changes
Other Study ID Numbers:	**CRFB002DDE13** 2010-018852-29 (EudraCT Number)
Study First Received:	May 25, 2010
Results First Received:	July 12, 2012
Last Updated:	August 20, 2012
Health Authority:	Germany: Paul-Ehrlich-Institut