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Trial record **1 of 1** for: CRFB002DES01

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Efficacy and Safety of Ranibizumab (Intravitreal Injections) Versus Laser Treatment in Patients With Visual Impairment Due to Diabetic Macular Edema (RED-ES)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT00901186

First received: May 11, 2009
Last updated: July 3, 2014
Last verified: July 2014
History of Changes

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Results First Received: May 30, 2014

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Conditions:	Diabetic Macular Edema Visual Impairment
Interventions:	Drug: RFB002 Procedure: Laser photocoagulation

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
No text entered.

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Participant Flow: Overall Study

	RFB002	Laser Photocoagulation
STARTED	**40**	**43**
Safety Set	**39** [1]	**43**
Intent to Treat	**35** [2]	**38** [3]
COMPLETED	**31**	**32**
NOT COMPLETED	**9**	**11**

Lack of Efficacy	**0**	**1**
Abnormal laboratory values	**0**	**1**
Lost to Follow-up	**2**	**0**
Adverse Event	**2**	**4**
Administration problems	**0**	**1**
Protocol deviations	**5**	**4**

[1] One participant did not receive one intravitreal RFB002 injection.
[2] Four treated participants did not have at least a baseline and one post-treatment BCVA.
[3] Five treated participants did not have at least a baseline and one post-treatment BCVA.

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
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.
Total	Total of all reporting groups

Baseline Measures

	RFB002	Laser Photocoagulation	Total
Number of Participants [units: participants]	**39**	**43**	**82**
Age [units: Years] Mean (Standard Deviation)	**61.31 (8.94)**	**65.47 (9.40)**	**63.49 (9.36)**
Gender [units: Participants]			
Female	**15**	**18**	**33**
Male	**24**	**25**	**49**

Outcome Measures

Hide All Outcome Measures

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

Measure Type	Primary
Measure Title	Mean Change From Baseline in Best Corrected Visual Acuity (BCVA)
Measure Description	Visual acuity (VA) was assessed on the study eye during every study visit using best correction determined from protocol refraction. VA measurements 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, 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.
Intent-to-treat (ITT): The ITT consisted of all randomized participants who received at least one intravitreal ranibizumab injection of one laser photocoagulation treatment for whom there was at least one baseline and one post-treatment BCVA value. Participants who had both Baseline and Month 12 BCVA values only were included in this analysis.

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Measured Values

	RFB002	**Laser Photocoagulation**
Number of Participants Analyzed [units: participants]	**32**	**33**
Mean Change From Baseline in Best Corrected Visual Acuity (BCVA) [units: letters] Mean (Standard Deviation)	**9.41 (9.15)**	**5.79 (9.40)**

No statistical analysis provided for Mean Change From Baseline in Best Corrected Visual Acuity (BCVA)

2. Secondary: Percentage of Participants With Improvement in BCVA [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Percentage of Participants With Improvement in BCVA
Measure Description	Visual acuity (VA) was assessed on the study eye during every study visit using best correction determined from

	protocol refraction. VA measurements 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	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.
Intent-to-treat (ITT): The ITT consisted of all randomized participants who received at least one intravitreal ranibizumab injection of one laser photocoagulation treatment for whom there was at least one baseline and one post-treatment BCVA value.

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Measured Values

	RFB002	**Laser Photocoagulation**
Number of Participants Analyzed [units: participants]	**35**	**38**
Percentage of Participants With Improvement in BCVA [units: Percentage of participants]	**74.29**	**68.42**

No statistical analysis provided for Percentage of Participants With Improvement in BCVA

3. Secondary: Evolution of Mean Change From Baseline in BCVA by Study Visit [Time Frame: Baseline, Months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12]

Measure Type	Secondary
Measure Title	Evolution of Mean Change From Baseline in BCVA by Study Visit
Measure Description	Visual acuity (VA) was assessed on the study eye during every study visit using best correction determined from protocol refraction. VA measurements 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, Months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 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.
ITT: The ITT consisted of all randomized participants who received at least one intravitreal ranibizumab injection of one laser photocoagulation treatment for whom there was at least one baseline and one post-treatment BCVA value. For each month, participants who had both the baseline and the study month BCVA values were included in the analysis.

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Measured Values

	RFB002	**Laser Photocoagulation**
Number of Participants Analyzed	**35**	**38**

[units: participants]		
Evolution of Mean Change From Baseline in BCVA by Study Visit [units: letters] Mean (Standard Deviation)		
Month 1 (n=34,38)	**4.56 (7.38)**	**1.32 (7.99)**
Month 2 (n=31,38)	**4.61 (6.55)**	**1.89 (8.04)**
Month 3 (n=33,38)	**6.24 (6.41)**	**3.11 (7.83)**
Month 4 (n=33,37)	**6.33 (7.40)**	**2.76 (8.66)**
Month 5 (n=31,37)	**7.03 (8.00)**	**3.38 (8.95)**
Month 6 (n=33,35)	**7.61 (6.88)**	**4.11 (7.65)**
Month 7 (n=33,33)	**7.91 (7.16)**	**3.85 (7.97)**
Month 8 (n=32,34)	**8.00 (7.77)**	**3.21 (7.75)**
Month 9 (n=32,33)	**8.44 (8.78)**	**6.00 (9.81)**
Month 10 (n=31,32)	**7.32 (8.17)**	**5.84 (9.14)**
Month 11 (n=32,32)	**7.69 (8.88)**	**6.44 (8.32)**
Month 12 (n=32,33)	**9.41 (9.15)**	**5.79 (9.40)**

No statistical analysis provided for Evolution of Mean Change From Baseline in BCVA by Study Visit

4. Secondary: Percentage of Participants With VA > 73 Letters With Ranibizumab (0.5 mg) vs Laser. [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Percentage of Participants With VA > 73 Letters With Ranibizumab (0.5 mg) vs Laser.
Measure Description	VA score was based on the number of letters read correctly on the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart assessed at a starting distance of 4 meters.

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.
Intent-to-treat (ITT): The ITT consisted of all randomized participants who received at least one intravitreal ranibizumab injection of one laser photocoagulation treatment for whom there was at least one baseline and one post-treatment BCVA value.

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Measured Values

	RFB002	**Laser Photocoagulation**
Number of Participants Analyzed [units: participants]	**35**	**38**
Percentage of Participants With VA > 73 Letters With Ranibizumab (0.5 mg) vs Laser. [units: Percentage of participants]	**54.29**	**23.68**

No statistical analysis provided for Percentage of Participants With VA > 73 Letters With Ranibizumab (0.5 mg) vs Laser.

5. Secondary: Mean Change From Baseline in Central Retinal Thickness (CRT) by Study Visit [Time Frame: Baseline, Months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12]

Measure Type	Secondary
Measure Title	Mean Change From Baseline in Central Retinal Thickness (CRT) by Study Visit
Measure Description	CRT was assessed by Optical Coherence Tomography (OCT).
Time Frame	Baseline, Months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 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.
ITT: The ITT consisted of all randomized participants who received at least one intravitreal ranibizumab injection of one laser photocoagulation treatment for whom there was at least one baseline and one post-treatment BCVA value. For each month, participants who had both the baseline and the study month CRT values were included in the analysis.

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Measured Values

	RFB002	**Laser Photocoagulation**
Number of Participants Analyzed [units: participants]	**35**	**38**
Mean Change From Baseline in Central Retinal Thickness (CRT) by Study Visit [units: micrometers]		

Mean (Standard Deviation)		
Month 1 (n=33,37)	-50.18 (62.23)	-21.86 (82.86)
Month 2 (n=31,38)	-69.52 (65.10)	-14.21 (66.95)
Month 3 (n=33,37)	-80.64 (87.06)	-43.16 (89.74)
Month 4 (n=33,38)	-81.79 (92.14)	-37.66 (83.29)
Month 5 (n=30,37)	-77.77 (73.47)	-28.92 (91.51)
Month 6 (n=33,34)	-93.73 (79.42)	-40.47 (100.12)
Month 7 (n=33,35)	-92.76 (79.55)	-60.94 (110.05)
Month 8 (n=32,34)	-92.41 (82.27)	-64.82 (110.05)
Month 9 (n=32,34)	-81.59 (81.38)	-74.59 (112.75)
Month 10 (n=31,31)	-83.32 (81.56)	-84.39 (102.79)
Month 11 (n=32,33)	-98.03 (76.75)	-94.85 (114.67)
Month 12 (n=32,33)	-76.28 (76.56)	-86.00 (115.53)

No statistical analysis provided for Mean Change From Baseline in Central Retinal Thickness (CRT) by Study Visit

6. Secondary: Percentage of CRT Change From Baseline by Study Visit [Time Frame: Baseline, Months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12]

Measure Type	Secondary
Measure Title	Percentage of CRT Change From Baseline by Study Visit
Measure Description	CRT was assessed by Optical Coherence Tomography (OCT).
Time Frame	Baseline, Months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 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.
ITT: The ITT consisted of all randomized participants who received at least one intravitreal ranibizumab injection of one laser photocoagulation treatment for whom there was at least one baseline and one post-treatment BCVA value. For each month, participants who had both the baseline and the study month CRT values were included in the analysis.

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Measured Values

	RFB002	**Laser Photocoagulation**
Number of Participants Analyzed [units: participants]	**35**	**38**
Percentage of CRT Change From Baseline by Study Visit [units: Percentage change] Mean (Standard Deviation)		
Month 1 (n=33,37)	**-12.06 (15.16)**	**-3.01 (17.52)**
Month 2 (n=31,38)	**-15.61 (13.90)**	**-2.20 (15.24)**
Month 3 (n=33,37)	**-18.25 (17.09)**	**-7.97 (17.80)**
Month 4 (n=33,38)	**-18.00 (17.93)**	**-6.99 (17.18)**
Month 5 (n=30,37)	**-18.21 (15.68)**	**-6.39 (19.27)**
Month 6 (n=33,34)	**-20.69 (15.85)**	**-8.55 (21.06)**

Month 7 (n=33,35)	**-21.11 (15.68)**	**-12.50 (23.05)**
Month 8 (n=32,34)	**-21.20 (16.43)**	**-13.02 (20.95)**
Month 9 (n=32,34)	**-19.17 (17.95)**	**-15.68 (21.87)**
Month 10 (n=31,31)	**-19.55 (17.34)**	**-17.24 (19.63)**
Month 11 (n=32,33)	**-22.65 (15.85)**	**-19.04 (22.31)**
Month 12 (n=32,33)	**-18.23 (16.66)**	**-16.59 (25.06)**

No statistical analysis provided for Percentage of CRT Change From Baseline by Study Visit

Serious Adverse Events

Hide Serious Adverse Events

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

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Serious Adverse Events

	RFB002	Laser Photocoagulation
Total, serious adverse events		

# participants affected / at risk	**3/39 (7.69%)**	**2/43 (4.65%)**
Cardiac disorders		
Cardiac failure acute † 1		
# participants affected / at risk	**1/39 (2.56%)**	**0/43 (0.00%)**
Cardiac failure congestive † 1		
# participants affected / at risk	**0/39 (0.00%)**	**1/43 (2.33%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Penile cancer † 1		
# participants affected / at risk	**0/39 (0.00%)**	**1/43 (2.33%)**
Nervous system disorders		
Cerebral infarction † 1		
# participants affected / at risk	**1/39 (2.56%)**	**0/43 (0.00%)**
Vascular disorders		
Necrosis ischaemic † 1		
# participants affected / at risk	**1/39 (2.56%)**	**0/43 (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	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
RFB002	RFB002 0.5 mg was administered to the study eye with a single monthly intravitreal injection on day 1, day 30 and day 60. After day 90, if stable vision was not achieved, a monthly injection of RFB002 0.5 mg was administered until stable vision was achieved.
Laser Photocoagulation	At least one treatment of laser photocoagulation was applied on day 1. The maximum number of laser photocoagulation treatments was 4.

Other Adverse Events

	RFB002	Laser Photocoagulation
Total, other (not including serious) adverse events		
# participants affected / at risk	**2/39 (5.13%)**	**3/43 (6.98%)**
Infections and infestations		
Pharyngitis † [1]		
# participants affected / at risk	**2/39 (5.13%)**	**0/43 (0.00%)**
Surgical and medical procedures		
Cataract operation † [1]		
# participants affected / at risk	**0/39 (0.00%)**	**3/43 (6.98%)**

† 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 or disclosure of trial results in their entirety.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 1-862-778-8300

No publications provided

Responsible Party:	Novartis (Novartis Pharmaceuticals)
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Other Study ID Numbers:	**CRFB002DES01** 2009-010825-37 (EudraCT Number)
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Results First Received:	May 30, 2014
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Health Authority:	Spain: Spanish Agency of Medicines