A Study of Ranibizumab Injection in Subjects With Clinically Significant Macular Edema (ME) With Center Involvement Secondary to Diabetes Mellitus (RISE) (RISE)

ClinicalTrials.gov Identifier: NCT00473330

Recruitment Status : Completed
First Posted : May 15, 2007
Results First Posted : January 17, 2013
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Sponsor:
Genentech, Inc.

Genentech, Inc.

Study Description

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Brief Summary:

This study is a Phase III, double-masked, multicenter, randomized, sham injection-controlled study of the efficacy and safety of ranibizumab injection in patients with clinically significant macular edema with center involvement (CSME-CI) secondary to diabetes mellitus (Type 1 or 2). This study is identical in design to study NCT00473382 (Protocol ID FVF4168g).

The open-label extension phase of the study was stopped after receiving FDA approval of the study drug (ranibizumab) for diabetic macular edema.

Condition or disease	Intervention/treatment	Phase
Diabetes Mellitus Macular Edema	Drug: Ranibizumab Drug: Sham injection	Phase 3

Detailed Description:
This study is composed of 3 phases: (1) A 24-month controlled treatment period (monthly treatment with ranibizumab 0.3 mg, ranibizumab 0.5 mg, or sham injection) followed by (2) a 12-month treatment period in which patients randomized to the sham group who had not discontinued from treatment (still masked) could choose to receive monthly ranibizumab 0.5 mg while the 2 ranibizumab treatment groups continued on the same treatment they received in the first 2 years. Patients who had not discontinued treatment by Month 36 were eligible to continue treatment with ranibizumab 0.5 mg as needed (pro re nata, PRN) in (3) an extension phase of the study for up to 2 more years, resulting in up to 5 years possible total treatment time for some patients.

Study Design

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Study Type :
Interventional (Clinical Trial)

Actual Enrollment :
377 participants

Allocation:
Randomized

Intervention Model:

Masking:

Double (Participant, Investigator)

Primary Purpose:

Treatment

Official Title:

A Phase III, Double-masked, Multicenter, Randomized, Sham Injection-controlled Study of the Efficacy and Safety of Ranibizumab Injection in Subjects With Clinically Significant Macular Edema With Center Involvement Secondary to Diabetes Mellitus

Study Start Date :

June 2007

Actual Primary Completion Date :

November 2010

Actual Study Completion Date :

November 2012

Resource links provided by the National Library of Medicine

MedlinePlus related topics: Edema

Drug Information available for: Ranibizumab

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Ranibizumab 0.3 mg Patients received ranibizumab 0.3 mg monthly administered intravitreally for 36 months. Patients who had not discontinued treatment by Month 36 could enter the open-label extension phase to receive ranibizumab 0.5 mg as needed (pro re nata [PRN]) for up to 24 additional months.	Drug: Ranibizumab Sterile solution for intravitreal injection. Other Name: Lucentis

Arm	Intervention/treatment
Experimental: Ranibizumab 0.5 mg Patients received ranibizumab 0.5 mg monthly administered intravitreally for 36 months. Patients who had not discontinued treatment by Month 36 could enter the open-label extension phase to receive ranibizumab 0.5 mg as needed (pro re nata [PRN]) for up to 24 additional months.	Drug: Ranibizumab Sterile solution for intravitreal injection. Other Name: Lucentis
Sham Comparator: Sham injection/ranibizumab 0.5 mg Patients received a sham intravitreal injection monthly for 24 months. Patients who had not discontinued treatment by Month 24 could choose to receive ranibizumab 0.5 mg monthly administered intravitreally for the subsequent 12 months. Patients who had not discontinued treatment by Month 36 could enter the open-label extension phase to receive ranibizumab 0.5 mg as needed (pro re nata [PRN]) for up to 24 additional months.	Drug: Sham injection

Outcome Measures

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Primary Outcome Measures :

1. Percentage of Patients Who Gained ≥ 15 Letters in Their Best Corrected Visual Acuity (BCVA) Score From Baseline at Month 24 [Time Frame: Baseline to Month 24]

   BCVA was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity (VA) chart starting at a test distance of 4 meters. The BCVA score is the number of letters read correctly by the patient. An increase in the BCVA score indicates an improvement of vision.

Secondary Outcome Measures :

1. Mean Change From Baseline in Best Corrected Visual Acuity (BCVA) Score at Months 24, 36, and 48 [Time Frame: Baseline to Month 48]

   BCVA was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity

correctly by the patient. An increase in the BCVA score indicates an improvement of vision. A positive change score indicates improvement.

2. Percentage of Patients With a Visual Acuity (VA) Snellen Equivalent of 20/40 or Better at Months 24, 36, and 48 [Time Frame: Months 24, 36, and 48]

   VA was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart starting at a test distance of 4 meters. An increase in the number of lines read correctly by the patient in the ETDRS chart indicates an improvement of vision. The Snellen equivalent of 20/40 or better is 69 or more letters correctly read in the EDTRS chart.

3. Percentage of Patients Who Lost < 15 Letters in Their Best Corrected Visual Acuity (BCVA) Score From Baseline at Months 24, 36, and 48 [Time Frame: Baseline to Month 48]

   BCVA was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity (VA) chart starting at a test distance of 4 meters. The BCVA score is the number of letters read correctly by the patient. An increase in the BCVA score indicates an improvement of vision.

4. Mean Change From Baseline in Best Corrected Visual Acuity (BCVA) Score at Months 24 and 36 in Patients With Focal Edema at Baseline [Time Frame: Baseline to Month 36]

   BCVA was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity (VA) chart starting at a test distance of 4 meters. The BCVA score is the number of letters read correctly by the patient. An increase in the BCVA score indicates an improvement of vision. A positive change score indicates improvement.

5. Mean Change From Baseline in Central Foveal Thickness at Months 24, 36, and 48 [Time Frame: Baseline to Month 48]

   Central foveal thickness was assessed in optical coherence tomographic images by the central reading center. A decrease in foveal thickness suggests a reduction in macular edema. A negative change score indicates improvement.

6. Percentage of Patients With a ≥ 3-step Worsening From Baseline in the Early Treatment Diabetic Retinopathy Study (ETDRS) Diabetic Retinopathy Severity Scale Score for Eyes at Months 24 and 36 [Time Frame: Baseline to Month 36]

   The severity of diabetic retinopathy was graded on a 10-point scale by the central reading center by comparing patient fundus photographic images with a set of standard images. 1=diabetic retinopathy (DR) severity level 10, 12 (DR absent), 2=DR severity level 14A-14C, 14Z, 15, 20 (DR questionable, microaneurysms only), 3=DR severity level 35A-35F (mild non-proliferative [NP]DR), 4=DR severity level 43A-43B (moderate NPDR), 5=DR severity level 47A-47D (moderately severe NPDR), 6=DR

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