

COVID-19 Information

[Public health information \(CDC\)](#)

[Research information \(NIH\)](#)

[SARS-CoV-2 data \(NCBI\)](#)

[Prevention and treatment information \(HHS\)](#)

[Español](#)

Try the modernized [ClinicalTrials.gov beta](#) website. Learn more about the [modernization effort](#).

NIH U.S. National Library of Medicine

ClinicalTrials.gov



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



The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT00473382

[Recruitment Status](#) ⓘ : Completed

[First Posted](#) ⓘ : May 15, 2007

[Results First Posted](#) ⓘ : January 17, 2013

[Last Update Posted](#) ⓘ : April 17, 2017

Sponsor:

Genentech, Inc.

Information provided by (Responsible Party):

Samsung v. Regeneron
IPR2023-00442
U.S. Pat. 10,130,681
Exhibit 2113

Genentech, Inc.

[Study Details](#)[Tabular View](#)[Study Results](#)[Disclaimer](#)[How to Read a Study Record](#)

Study Description

Go to 

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 NCT00473330 (Protocol ID FVF4170g).

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	Drug: Ranibizumab	Phase 3
Macular Edema	Drug: Sham injection	

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.

As per the protocol, Genentech terminated the study approximately 30 days after approval of ranibizumab for diabetic macular edema in the United States.

Study Design

Go to 

[Study Type](#) ⓘ :

Interventional (Clinical Trial)

[Actual Enrollment](#) ⓘ :

382 participants

Allocation:

Randomized

Intervention Model:

Parallel Assignment

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 ⓘ :

January 2011

Actual Study Completion Date ⓘ :

September 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**Go to

Arm ⓘ	Intervention/treatment ⓘ
-----------------------	--

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
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

Go to 

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 (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.

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 severity level 53A-53E (severe NPDR), 7=DR severity level 60, 61A, 61B (mild proliferative [P]DR), 8=DR severity level 65A-65C (moderate PDR), 9=DR severity level 71A-71D (high-risk PDR), 10=DR severity level 90 (cannot grade). A lower score indicates less severe diabetic retinopathy.

7. Percentage of Patients With Resolution of Leakage at Month 24 [Time Frame: Baseline to Month 24]

Resolution of leakage was defined as total area of fluorescein leakage in the central, inner, and outer subfields of the 0 Disc Area. Leakage was assessed in fluorescein angiographic images by the central reading center.

8. Mean Number of Macular Laser Treatments From Baseline Through Months 24 and 36 [Time Frame: Baseline to Month 36]

The need for macular laser treatment was evaluated by the masked (evaluating) physician. Macular laser was administered per protocol-specified objective and subjective criteria starting at Month 3.

9. Percentage of Patients Who Gained ≥ 15 Letters in Their Best Corrected Visual Acuity (BCVA) Score From Baseline at Months 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.

10. Mean Change From Month 36 in Best Corrected Visual Acuity (BCVA) Score in the Study Eye at Month 48 [Time Frame: Month 36 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. A positive change score indicates improvement.

11. Percentage of Patients Who Lost < 15 Letters in Their Best Corrected Visual Acuity (BCVA) Score in the Study Eye From Month 36 at Month 48 [Time Frame: Month 36 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.

12. Mean Change From Month 36 in Central Foveal Thickness in the Study Eye at Month 48 [Time Frame: Month 36 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.

Eligibility Criteria

Go to 

Information from the National Library of Medicine



Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, [Learn About Clinical Studies](#).

Ages Eligible for Study:

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study:

All

Accepts Healthy Volunteers:

No

Criteria

Inclusion Criteria:

- Willingness to provide written informed consent and, at U.S. sites, Health Insurance Portability and Accountability Act (HIPAA) authorization, and in other countries, as applicable according to national laws.
- Age $\geq$ 18 years.
- Diabetes mellitus (Type 1 or 2) .

- Retinal thickening secondary to diabetes mellitus (DME) involving the center of the fovea with central macular thickness ≥ 275 μm in the center subfield as assessed on optical coherence tomography (OCT).
- Best corrected visual acuity (BCVA) score in the study eye of 20/40 to 20/320 approximate Snellen equivalent using the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol at an initial testing distance of 4 meters.
- Decrease in vision determined to be primarily the result of DME and not to other causes.
- For sexually active women of childbearing potential, use of an appropriate form of contraception (or abstinence) for the duration of the study.
- Ability (in the opinion of the investigator) and willingness to return for all scheduled visits and assessments.

Exclusion Criteria:

- History of vitreoretinal surgery in the study eye.
- Panretinal photocoagulation (PRP) or macular laser photocoagulation in the study eye within 3 months of screening.
- Previous use of intraocular corticosteroids in the study eye (eg, triamcinolone acetonide [TA]) within 3 months of screening.
- Previous treatment with anti-angiogenic drugs in either eye (pegaptanib sodium, anecortave acetate, bevacizumab, ranibizumab, etc) within 3 months of the Day 0 (first day of treatment) visit.
- Proliferative diabetic retinopathy (PDR) in the study eye, with the exception of inactive, regressed PDR.
- Iris neovascularization, vitreous hemorrhage, traction retinal detachment, or preretinal fibrosis involving the macula in the study eye.

Concurrent Ocular Conditions

- Vitreomacular traction or epiretinal membrane in the study eye.
- Ocular inflammation (including trace or above) in the study eye.
- History of idiopathic or autoimmune uveitis in either eye.
- Structural damage to the center of the macula in the study eye that is likely to preclude improvement in VA following the resolution of macular edema, including atrophy of the retinal pigment epithelium (RPE), subretinal fibrosis, or organized hard-exudate plaque.
- Ocular disorders in the study eye that may confound interpretation of study results, including retinal vascular occlusion, retinal detachment, macular hole, or choroidal neovascularization (CNV) of any cause (eg, age-related macular degeneration (AMD), ocular histoplasmosis, or pathologic myopia).
- Concurrent disease in the study eye that would compromise visual acuity or require medical or surgical intervention during the study period.
- Cataract surgery in the study eye within 3 months, yttrium-aluminum-garnet (YAG) laser capsulotomy within the past 2 months, or any other intraocular surgery within the 90 days preceding Day 0.
- Aphakia or absence of the posterior capsule in the study eye.

- Uncontrolled glaucoma or previous filtration surgery in the study eye.
- Spherical equivalent of the refractive error in the study eye of more than -8 diopters myopia.
- Evidence at examination of infectious blepharitis, keratitis, scleritis, or conjunctivitis in either eye or current treatment for serious systemic infection.
- Uncontrolled blood pressure.
- History of cerebral vascular accident or myocardial infarction within 3 months prior to Day 0.
- Uncontrolled diabetes mellitus.
- Renal failure requiring dialysis or renal transplant.
- Participation in an investigational trial within 30 days prior to screening that involved treatment with any drug (excluding vitamins and minerals) or device.
- History of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use an investigational drug, might affect interpretation of the results of the study, or renders the subject at high risk from treatment complications.
- Pregnancy or lactation.
- History of allergy to fluorescein.
- History of allergy to ranibizumab injection or related molecule.

Contacts and Locations

Go to 

Information from the National Library of Medicine



To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

*Please refer to this study by its ClinicalTrials.gov identifier (NCT number): **NCT00473382***

Sponsors and Collaborators

Genentech, Inc.

Investigators

Study Director: Jason Ehrlich, M.D., Ph.D. Genentech, Inc.

More Information

Go to 

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Exhibit 2113

[Gonzalez VH, Wang PW, Ruiz CQ. Panretinal Photocoagulation for Diabetic Retinopathy in the RIDE and RISE Trials: Not "1 and Done". Ophthalmology. 2021 Oct;128\(10\):1448-1457. doi: 10.1016/j.ophtha.2019.08.010. Epub 2019 Aug 21.](#)

[Wykoff CC, Eichenbaum DA, Roth DB, Hill L, Fung AE, Haskova Z. Ranibizumab Induces Regression of Diabetic Retinopathy in Most Patients at High Risk of Progression to Proliferative Diabetic Retinopathy. Ophthalmol Retina. 2018 Oct;2\(10\):997-1009. doi: 10.1016/j.oret.2018.06.005. Epub 2018 Aug 1.](#)

[Sun JK, Wang PW, Taylor S, Haskova Z. Durability of Diabetic Retinopathy Improvement with As-Needed Ranibizumab: Open-Label Extension of RIDE and RISE Studies. Ophthalmology. 2019 May;126\(5\):712-720. doi: 10.1016/j.ophtha.2018.10.041. Epub 2018 Nov 9.](#)

[Reddy RK, Pieramici DJ, Gune S, Ghanekar A, Lu N, Quezada-Ruiz C, Bauman CR. Efficacy of Ranibizumab in Eyes with Diabetic Macular Edema and Macular Nonperfusion in RIDE and RISE. Ophthalmology. 2018 Oct;125\(10\):1568-1574. doi: 10.1016/j.ophtha.2018.04.002. Epub 2018 May 8.](#)

[Moshfeghi AA, Shapiro H, Lemmon LA, Gune S. Impact of Cataract Surgery during Treatment with Ranibizumab in Patients with Diabetic Macular Edema. Ophthalmol Retina. 2018 Feb;2\(2\):86-90. doi: 10.1016/j.oret.2017.05.003. Epub 2017 Jul 27.](#)

[Singh RP, Habbu K, Ehlers JP, Lansang MC, Hill L, Stoilov I. The Impact of Systemic Factors on Clinical Response to Ranibizumab for Diabetic Macular Edema. Ophthalmology. 2016 Jul;123\(7\):1581-7. doi: 10.1016/j.ophtha.2016.03.038. Epub 2016 May 24.](#)

[Pieramici DJ, Wang PW, Ding B, Gune S. Visual and Anatomic Outcomes in Patients with Diabetic Macular Edema with Limited Initial Anatomic Response to Ranibizumab in RIDE and RISE. Ophthalmology. 2016 Jun;123\(6\):1345-50. doi: 10.1016/j.ophtha.2016.02.007. Epub 2016 Mar 15.](#)

[Bressler NM, Varma R, Mitchell P, Suñer IJ, Dolan C, Ward J, Ferreira A, Ehrlich JS, Turpcu A. Effect of Ranibizumab on the Decision to Drive and Vision Function Relevant to Driving in Patients With Diabetic Macular Edema: Report From RESTORE, RIDE, and RISE Trials. JAMA Ophthalmol. 2016 Feb;134\(2\):160-6. doi: 10.1001/jamaophthalmol.2015.4636.](#)

[Boyer DS, Nguyen QD, Brown DM, Basu K, Ehrlich JS; RIDE and RISE Research Group. Outcomes with As-Needed Ranibizumab after Initial Monthly Therapy: Long-Term Outcomes of the Phase III RIDE and RISE Trials. Ophthalmology. 2015 Dec;122\(12\):2504-13.e1. doi: 10.1016/j.ophtha.2015.08.006. Epub 2015 Oct 9.](#)

[Bansal AS, Khurana RN, Wieland MR, Wang PW, Van Everen SA, Tuomi L. Influence of Glycosylated Hemoglobin on the Efficacy of Ranibizumab for Diabetic Macular Edema: A Post Hoc Analysis of the RIDE/RISE Trials. Ophthalmology. 2015 Aug;122\(8\):1573-9. doi: 10.1016/j.ophtha.2015.04.029. Epub 2015 Jun 4.](#)

[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.](#)

[Campochiaro PA, Wykoff CC, Shapiro H, Rubio RG, Ehrlich JS. Neutralization of vascular endothelial growth factor slows progression of retinal nonperfusion in patients with diabetic macular edema. Ophthalmology. 2014 Sep;121\(9\):1783-9. doi: 10.1016/j.ophtha.2014.03.021. Epub 2014 Apr 24.](#)

[Brown DM, Nguyen QD, Marcus DM, Boyer DS, Patel S, Feiner L, Schlottmann PG, Rundle AC, Zhang J, Rubio RG, Adamis AP, Ehrlich JS, Hopkins JJ; RIDE and RISE Research Group. Long-term outcomes of ranibizumab therapy for diabetic macular edema: the 36-month results from two phase III trials: RISE and RIDE. Ophthalmology. 2013 Oct;120\(10\):2013-22. doi: 10.1016/j.ophtha.2013.02.034. Epub 2013 May 22.](#)

[Ip MS, Domalpally A, Hopkins JJ, Wong P, Ehrlich JS. Long-term effects of ranibizumab on diabetic retinopathy severity and progression. Arch Ophthalmol. 2012 Sep;130\(9\):1145-52. doi: 10.1001/archophthalmol.2012.1043.](#)

Responsible Party:

Genentech, Inc.

ClinicalTrials.gov Identifier:

[NCT00473382](#) [History of Changes](#)

Other Study ID Numbers:

FVF4168g

First Posted:

May 15, 2007 [Key Record Dates](#)

Results First Posted:

January 17, 2013

Last Update Posted:

April 17, 2017

Last Verified:

March 2017

Keywords provided by Genentech, Inc.:

Lucentis
DME
Diabetes
Vision loss

Additional relevant MeSH terms:

Macular Edema
Diabetes Mellitus
Edema
Glucose Metabolism Disorders
Metabolic Diseases
Endocrine System Diseases
Macular Degeneration
Retinal Degeneration
Retinal Diseases
Eye Diseases
Ranibizumab
Angiogenesis Inhibitors
Angiogenesis Modulating Agents
Growth Substances
Physiological Effects of Drugs
Growth Inhibitors
Antineoplastic Agents