ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 07/15/2013

ClinicalTrials.gov ID: NCT00168324

Study Identification

Unique Protocol ID:	206207-008
Brief Title:	A Study of the Safety and Efficacy of a New Treatment for Macular Edema Resulting From Retinal Vein Occlusion
Official Title:	
Secondary IDs:	

Study Status

Record Verification:	July 2013
Overall Status:	Completed
Study Start:	October 2004
Primary Completion:	March 2008 [Actual]
Study Completion:	October 2008 [Actual]

Sponsor/Collaborators

Sponsor:	Allergan
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No

IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 58,663 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This study will evaluate the safety and efficacy of an intravitreal implant of dexamethasone for the treatment of macular edema associated with retinal vein occlusion.
Detailed Description:	

Conditions

Conditions:	Macular Edema Retinal Vein Occlusion
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	3
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 599 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 700 µg Dexamethasone 700 µg dexamethasone intravitreal implant administered on Day 0 and Day 180.	Drug: 700 µg Dexamethasone 700 µg dexamethasone intravitreal implant administered on Day 0 and/or Day 180. Other Names: • Posurdex®
Experimental: 350 µg Dexamethasone followed by 700 µg Dexamethasone 350 µg dexamethasone intravitreal implant administered on Day 0 and 700 µg dexamethasone intravitreal implant on Day 180.	Drug: 700 µg Dexamethasone 700 µg dexamethasone intravitreal implant administered on Day 0 and/or Day 180. Other Names: • Posurdex® Drug: 350 µg Dexamethasone 350 µg Dexamethasone intravitreal implant administered on Day 0. Other Names: • Posurdex®
Sham Comparator: Sham Injection followed by 700 µg Dexamethasone Sham injection on Day 0 and 700 µg dexamethasone intravitreal implant on Day 180.	Drug: 700 µg Dexamethasone 700 µg dexamethasone intravitreal implant administered on Day 0 and/or Day 180. Other Names: • Posurdex® Sham Injection Sham injection on Day 0.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- 18 years of age or older with macular edema resulting from retinal vein occlusion
- Decrease in visual acuity in at least one eye as a result of macular edema (20/50 or worse)
- Visual acuity in other eye no worse than 20/200

Exclusion Criteria:

- Known anticipated need for ocular surgery within next 12 months
- History of glaucoma or current high eye pressure requiring more than 1 medication
- Diabetic retinopathy
- Uncontrolled systemic disease
- Known steroid-responder
- Use of systemic steroids
- Use of warfarin/heparin

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc.

Locations: United States, California
Los Angeles, California, United States

Canada, Nova Scotia
Halifax, Nova Scotia, Canada

Australia
Sydney, Australia

South Africa
Arcadia, South Africa

Germany
Karlsruhe, Germany

Israel
Rehovot, Israel

Austria
Graz, Austria

Mexico

Tabacalera, Mexico

Portugal
Coimbra, Portugal

Czech Republic
Brno, Czech Republic

France
Creteil, France

Taiwan
Kaohsiung, Taiwan

Philippines
Makati, Philippines

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	Patients were randomly assigned during the double-blind period of the study to treatment with 700 µg dexamethasone, 350 µg dexamethasone, or sham injection on Day 0. Patients who qualified to continue in the open-label period of the study received 700 µg dexamethasone on Day 180.

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0 and Day 180.
350 µg Dexamethasone Followed by 700 µg Dexamethasone	350 µg dexamethasone intravitreal implant administered on Day 0 and 700 µg dexamethasone intravitreal implant on Day 180.

	Description
Sham Injection Followed by 700 µg Dexamethasone	Sham injection on Day 0 and 700 µg dexamethasone intravitreal implant on Day 180.

Double-Blind Period

	700 µg Dexamethasone	350 µg Dexamethasone Followed by 700 µg Dexamethasone	Sham Injection Followed by 700 µg Dexamethasone
Started	201	196	202
Completed	189	189	189
Not Completed	12	7	13

Open-Label Period

	700 µg Dexamethasone	350 µg Dexamethasone Followed by 700 µg Dexamethasone	Sham Injection Followed by 700 µg Dexamethasone
Started	164 [1]	155 [1]	158 [1]
Completed	160	147	152
Not Completed	4	8	6

[1] Not all patients who completed the double-blind period entered the open-label period.

Baseline Characteristics

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0 and Day 180.
350 µg Dexamethasone Followed by 700 µg Dexamethasone	350 µg dexamethasone intravitreal implant administered on Day 0 and 700 µg dexamethasone intravitreal implant on Day 180.
Sham Injection Followed by 700 µg Dexamethasone	Sham injection on Day 0 and 700 µg dexamethasone intravitreal implant on Day 180.

Baseline Measures

	700 µg Dexamethasone	350 µg Dexamethasone Followed by 700 µg Dexamethasone	Sham Injection Followed by 700 µg Dexamethasone	Total
Number of Participants	201	196	202	599
Age, Customized [units: participants]				
<45 years	9	7	9	25
45-65 years	83	84	90	257
>65 years	109	105	103	317
Gender, Male/Female [units: participants]				
Female	95	92	85	272
Male	106	104	117	327

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Cumulative Response Rate of 15 or More Letter Improvement
Measure Description	The cumulative response rate of 15 or more letter improvement was based on the Kaplan-Meier estimate. A Kaplan-Meier analysis takes into account patients who dropped out from the study prior to achieving the 15 letter improvement. Values ranged from 0-1, with a higher number indicating a higher probability of response.
Time Frame	Up to 180 Days
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: all randomized patients

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0.
350 µg Dexamethasone	350 µg Dexamethasone intravitreal implant administered on Day 0.
Sham Injection	Sham injection on Day 0.

Measured Values

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
Number of Participants Analyzed	201	196	202
Cumulative Response Rate of 15 or More Letter Improvement [units: Kaplan-Meier Estimate]			
Day 30	0.101	0.092	0.045
Day 60	0.258	0.204	0.100
Day 90	0.359	0.292	0.165
Day 180	0.397	0.349	0.225

2. Secondary Outcome Measure:

Measure Title	Number of Patients With 15 or More Letter Improvement in Best Corrected Visual Acuity (BCVA) in the Study Eye
Measure Description	BCVA is measured using an eye chart and is reported as the number of letters read correctly (ranging from 0 to 100 letters). The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). An increase in the number of letters read correctly means that vision has improved. The numbers of patients with at least a 15 or more letter improvement in BCVA in the study eye at each visit are presented.
Time Frame	Day 90, Day 180
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: all randomized patients

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0.
350 µg Dexamethasone	350 µg Dexamethasone intravitreal implant administered on Day 0.
Sham Injection	Sham injection on Day 0.

Measured Values

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
Number of Participants Analyzed	201	196	202

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
Number of Patients With 15 or More Letter Improvement in Best Corrected Visual Acuity (BCVA) in the Study Eye [units: Number of Participants]			
Day 90	45	41	25
Day 180	39	32	37

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Retinal Thickness in the Study Eye
Measure Description	Retinal thickness is assessed by optical coherence tomography (OCT) in the study eye. The retina is the light-sensitive part of the eye. OCT is a laser-based, noninvasive, diagnostic system providing high-resolution, three-dimensional images of the retina. A negative change from baseline indicates an improvement.
Time Frame	Baseline, Day 90, Day 180
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: all randomized patients

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0.
350 µg Dexamethasone	350 µg Dexamethasone intravitreal implant administered on Day 0.
Sham Injection	Sham injection on Day 0.

Measured Values

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
Number of Participants Analyzed	201	196	202
Change From Baseline in Retinal Thickness in the Study Eye [units: Microns (µm)] Mean (Standard Deviation)			
Baseline	548.9 (185.45)	541.6 (183.68)	534.4 (187.38)

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
Change from Baseline at Day 90	-199.3 (194.54)	-144.1 (166.59)	-78.2 (150.05)
Change from Baseline at Day 180	-105.0 (197.83)	-91.4 (198.16)	-110.3 (175.59)

4. Secondary Outcome Measure:

Measure Title	Percentage of Patients With a Change From Baseline in BCVA by Category
Measure Description	BCVA is measured using an eye chart and is reported as the number of letters read correctly (ranging from 0 to 100 letters). The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). An increase in the number of letters read correctly means that vision has improved. Data are grouped into the following 5 categories based on change from baseline: ≥15 Letters Improvement, ≥5 and <15 Letters Improvement, No Change (Between -5 to +5 Letters), ≥5 and <15 Letters Worsening, and ≥15 Letters Worsening.
Time Frame	Baseline, Day 90
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: all randomized patients

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0.
350 µg Dexamethasone	350 µg Dexamethasone intravitreal implant administered on Day 0.
Sham Injection	Sham injection on Day 0.

Measured Values

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
Number of Participants Analyzed	201	196	202
Percentage of Patients With a Change From Baseline in BCVA by Category [units: Percentage of Patients]			
≥15 Letters Improvement	22.4	20.9	12.4
≥5 and <15 Letters Improvement	39.8	42.3	34.2
No Change (Between -5 to +5 Letters)	27.4	23.5	34.7

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
≥5 and <15 Letters Worsening	7.0	9.2	13.4
≥15 Letters Worsening	3.5	4.1	5.4

5. Secondary Outcome Measure:

Measure Title	Percentage of Patients With a Change From Baseline in BCVA by Category
Measure Description	BCVA is measured using an eye chart and is reported as the number of letters read correctly (ranging from 0 to 100 letters). The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). An increase in the number of letters read correctly means that vision has improved. Data are grouped into the following 5 categories based on change from baseline: ≥15 Letters Improvement, ≥5 and <15 Letters Improvement, No Change (Between -5 to +5 Letters), ≥5 and <15 Letters Worsening, and ≥15 Letters Worsening.
Time Frame	Baseline, Day 180
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: all randomized patients

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0.
350 µg Dexamethasone	350 µg Dexamethasone intravitreal implant administered on Day 0.
Sham Injection	Sham injection on Day 0.

Measured Values

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
Number of Participants Analyzed	201	196	202
Percentage of Patients With a Change From Baseline in BCVA by Category [units: Percentage of Patients]			
≥15 Letters Improvement	19.4	16.3	18.3
≥5 and <15 Letters Improvement	34.8	37.8	27.7
No Change (Between -5 to +5 Letters)	29.4	25.5	30.2

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
≥5 and <15 Letters Worsening	10.9	10.7	14.9
≥15 Letters Worsening	5.5	9.7	8.9

Reported Adverse Events

Time Frame	Adverse Events (AEs) and Serious Adverse Events (SAEs) are reported for the double-blind treatment period through Month 6.
Additional Description	The safety population included all randomized patients who received at least one dose of study medication and was used to assess AEs and SAEs.

Reporting Groups

	Description
700 µg Dexamethasone	700 µg dexamethasone intravitreal implant administered on Day 0 and Day 180.
350 µg Dexamethasone	350 µg Dexamethasone intravitreal implant administered on Day 0.
Sham Injection	Sham injection on Day 0.

Serious Adverse Events

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	12/196 (6.12%)	28/197 (14.21%)	14/202 (6.93%)
Cardiac disorders			
Angina pectoris [A] *	2/196 (1.02%)	0/197 (0%)	0/202 (0%)
Arrhythmia [A] †	0/196 (0%)	2/197 (1.02%)	0/202 (0%)
Cardiac failure congestive [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Cardiogenic shock [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Coronary artery stenosis [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Myocardial infarction [A] †	1/196 (0.51%)	4/197 (2.03%)	0/202 (0%)

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Eye disorders			
Blindness [A] *	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Glaucoma [A] †	0/196 (0%)	1/197 (0.51%)	1/202 (0.5%)
Retinal vein occlusion [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Gastrointestinal disorders			
Pancreatitis [A] †	1/196 (0.51%)	0/197 (0%)	0/202 (0%)
Small intestinal obstruction [A] †	1/196 (0.51%)	0/197 (0%)	0/202 (0%)
General disorders			
Chest pain [A] *	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Drowning [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Infections and infestations			
Gastroenteritis [A] *	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Pneumonia [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Pneumonia viral [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Urinary tract infection [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Injury, poisoning and procedural complications			
Humerus fracture [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Investigations			
Blood pressure increased [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Intraocular pressure increased [A] †	1/196 (0.51%)	3/197 (1.52%)	0/202 (0%)
Musculoskeletal and connective tissue disorders			
Osteoarthritis [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Spinal osteoarthritis [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Lung adenocarcinoma [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Squamous cell carcinoma [A] †	1/196 (0.51%)	0/197 (0%)	0/202 (0%)
Nervous system disorders			
Carotid artery stenosis [A] †	1/196 (0.51%)	0/197 (0%)	0/202 (0%)
Cerebrovascular accident [A] †	1/196 (0.51%)	1/197 (0.51%)	0/202 (0%)
Convulsion [A] *	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Syncope [A] *	0/196 (0%)	1/197 (0.51%)	2/202 (0.99%)
Thrombotic stroke [A] †	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Transient ischaemic attack [A] †	1/196 (0.51%)	1/197 (0.51%)	1/202 (0.5%)
Psychiatric disorders			
Mental status changes [A] †	1/196 (0.51%)	0/197 (0%)	0/202 (0%)
Renal and urinary disorders			
Renal colic [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Renal failure acute [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Reproductive system and breast disorders			
Benign prostatic hyperplasia [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Respiratory, thoracic and mediastinal disorders			
Dyspnoea [A] *	0/196 (0%)	0/197 (0%)	1/202 (0.5%)
Pulmonary embolism [A] †	1/196 (0.51%)	0/197 (0%)	0/202 (0%)
Respiratory failure [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)
Vascular disorders			

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hypotension [A] †	0/196 (0%)	1/197 (0.51%)	0/202 (0%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA version 11.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	700 µg Dexamethasone	350 µg Dexamethasone	Sham Injection
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	119/196 (60.71%)	107/197 (54.31%)	63/202 (31.19%)
Eye disorders			
Conjunctival haemorrhage [A] †	39/196 (19.9%)	35/197 (17.77%)	26/202 (12.87%)
Conjunctival hyperaemia [A] †	10/196 (5.1%)	11/197 (5.58%)	7/202 (3.47%)
Eye pain [A] *	13/196 (6.63%)	8/197 (4.06%)	7/202 (3.47%)
Maculopathy [A] †	11/196 (5.61%)	7/197 (3.55%)	17/202 (8.42%)
Investigations			
Intraocular pressure increased [A] †	46/196 (23.47%)	46/197 (23.35%)	6/202 (2.97%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA version 11.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

A 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 90 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

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