ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 08/01/2012

ClinicalTrials.gov ID: NCT00511706

Study Identification

Unique Protocol ID:	206207-016
Brief Title:	Safety and Efficacy of a New Treatment as Adjunctive Therapy to Anti-vascular Endothelial Growth Factor (Anti-VEGF) Treatment in Patients With Age-Related Macular Degeneration (AMD)
Official Title:	
Secondary IDs:	

Study Status

Record Verification:	August 2012
Overall Status:	Completed
Study Start:	November 2007
Primary Completion:	March 2009 [Actual]
Study Completion:	March 2009 [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:	The study will evaluate the safety and efficacy of the intravitreal implant of dexamethasone with Anti-VEGF treatment vs. Anti-VEGF alone (with sham dexamethasone injection) in patients with subfoveal choroidal neovascularization secondary to age-related macular degeneration.
Detailed Description:	

Conditions

Conditions:	Choroidal Neovascularization Age-Related Maculopathy
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	2

Masking:	Double Blind (Subject, Caregiver, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	243 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: dexamethasone and ranibizumab Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.	Drug: dexamethasone Intravitreal injection of dexamethasone 700 µg at Day 1. Other Names: • Posurdex Biological/Vaccine: ranibizumab Ranibizumab 500 µg at day -30 and Day 7-14. Other Names: • Lucentis®
Sham Comparator: sham and ranibizumab Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.	Biological/Vaccine: ranibizumab Ranibizumab 500 µg at day -30 and Day 7-14. Other Names: • Lucentis® sham Sham needle-less injection administered in the study eye at Day 1.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	50 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- 50 years of age or older with subfoveal choroidal neovascularization (CNV) (classic and/or occult) secondary to AMD
- Visual Acuity between 20/40 and 20/400 in the study eye

Exclusion Criteria:

- Any intraocular surgery within 3 months
- Glaucoma
- Cataract
- High eye pressure
- Uncontrolled systemic disease

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc.

Locations: United States, Florida
Boynton Beach, Florida, United States

Australia, New South Wales
Parramatta, New South Wales, Australia

Israel
Tel Aviv, Israel

Italy
Milano, Italy

New Zealand
Auckland, New Zealand

France
Paris, France

United Kingdom
Southampton, Hampshire, United Kingdom

Portugal
Coimbra, Portugal

Korea, Republic of
Seoul, Korea, Republic of

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Dexamethasone and Ranibizumab	Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.
Sham and Ranibizumab	Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.

Overall Study

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
Started	123	120
Completed	115	115
Not Completed	8	5

Baseline Characteristics

Reporting Groups

	Description
Dexamethasone and Ranibizumab	Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.
Sham and Ranibizumab	Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.

Baseline Measures

	Dexamethasone and Ranibizumab	Sham and Ranibizumab	Total
Number of Participants	123	120	243

	Dexamethasone and Ranibizumab	Sham and Ranibizumab	Total
Age, Continuous [units: Years] Mean (Standard Deviation)	76.1 (8.83)	76.2 (8.50)	76.1 (8.65)
Gender, Male/Female [units: Participants]			
Female	76	69	145
Male	47	51	98

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Injection Free Interval
Measure Description	The injection free interval was defined as the number of days between receiving the second ranibizumab injection (day 7 to 14) to the investigator's determination of eligibility to receive a third ranibizumab injection in the study eye.
Time Frame	Week 1 to Week 25
Safety Issue?	No

Analysis Population Description

Intent-to-treat population consisted of all randomized patients.

Reporting Groups

	Description
Dexamethasone and Ranibizumab	Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.
Sham and Ranibizumab	Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.

Measured Values

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
Number of Participants Analyzed	123	120
Injection Free Interval [units: Days] Median (Inter-Quartile Range)	34 (28 to 85)	29 (28 to 56)

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Best Corrected Visual Acuity (BCVA) at Week 25
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) in the study eye. 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.
Time Frame	Baseline, Week 25
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population (all randomized patients) with data available at Baseline and Week 25 for analyses.

Reporting Groups

	Description
Dexamethasone and Ranibizumab	Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.
Sham and Ranibizumab	Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.

Measured Values

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
Number of Participants Analyzed	122	120
Change From Baseline in the Best Corrected Visual Acuity (BCVA) at Week 25 [units: Letters] Mean (Standard Deviation)		
Baseline	55.5 (15.27)	58.1 (12.64)
Change from baseline at week 25	2.0 (8.61)	2.4 (9.14)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Mean Central Retinal Subfield Thickness at Week 25 as Assessed by Optical Coherence Tomography (OCT) in the Study Eye
Measure Description	Optical Coherence Tomography (OCT), a laser based non-invasive diagnostic system providing high-resolution imaging sections of the retina, was performed in the study eye after pupil dilation at baseline and Month 25.
Time Frame	Baseline, Week 25
Safety Issue?	No

Analysis Population Description

Participants from the Intent-to-treat population (all randomized patients) with data available at Baseline and Week 25 for analyses.

Reporting Groups

	Description
Dexamethasone and Ranibizumab	Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.
Sham and Ranibizumab	Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.

Measured Values

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
Number of Participants Analyzed	120	119
Change From Baseline in the Mean Central Retinal Subfield Thickness at Week 25 as Assessed by Optical Coherence Tomography (OCT) in the Study Eye [units: Microns] Mean (Standard Deviation)		
Baseline	260.28 (123.625)	272.45 (130.829)
Change from baseline at week 25 (n=105, 111)	-7.12 (77.898)	-13.00 (97.651)

4. Secondary Outcome Measure:

Measure Title	Change From Screening in the Area of Leakage From Choroidal Neovascularization (CNV) at Week 25 as Assessed by Fluorescein Angiography in the Study Eye
Measure Description	Fluorescein angiography (FA) is a technique for examining the circulation of the retina (and detecting any leakage) using a dye-tracing method. Photographs are taken with a specialized low-power microscope with an attached camera designed to photograph the interior of the eye, including the retina and optic disc. FA was performed on the study eye after dilation at Screening and Week 25.
Time Frame	Screening (-Week 28), Week 25
Safety Issue?	No

Analysis Population Description

Participants from the intent-to-treat population (all randomized participants) with data available at Screening and Week 25 for analyses.

Reporting Groups

	Description
Dexamethasone and Ranibizumab	Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.
Sham and Ranibizumab	Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.

Measured Values

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
Number of Participants Analyzed	118	116
Change From Screening in the Area of Leakage From Choroidal Neovascularization (CNV) at Week 25 as Assessed by Fluorescein Angiography in the Study Eye [units: Millimeters square (MM^2)] Mean (Standard Deviation)		
Screening	8.44 (6.863)	8.12 (6.359)
Change from Screening at Week 25 (n= 95,99)	-2.32 (4.927)	-1.73 (5.465)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	Safety population was used to calculate the number of participants at risk for Serious Adverse Events and Adverse Events and was defined as all randomized participants who received study drug.

Reporting Groups

	Description
Dexamethasone and Ranibizumab	Intravitreal injection of dexamethasone 700 µg at Day 1; ranibizumab 500 µg at Day -30 and Day 7-14.
Sham and Ranibizumab	Sham injection at Day 1; ranibizumab 500 µg at day -30 and Day 7-14.

Serious Adverse Events

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
	Affected/At Risk (%)	Affected/At Risk (%)
Total	9/121 (7.44%)	14/118 (11.86%)
Cardiac disorders		
Atrial fibrillation [A] †	0/121 (0%)	2/118 (1.69%)
Atrioventricular block complete [A] †	0/121 (0%)	1/118 (0.85%)
Bradycardia [A] †	1/121 (0.83%)	0/118 (0%)
Cardiac failure chronic [A] †	0/121 (0%)	1/118 (0.85%)
Ischaemic cardiomyopathy [A] †	0/121 (0%)	1/118 (0.85%)
Mitral valve incompetence [A] †	0/121 (0%)	1/118 (0.85%)
Myocardial infarction [A] †	1/121 (0.83%)	2/118 (1.69%)
Gastrointestinal disorders		
Duodenal ulcer perforation [A] †	0/121 (0%)	1/118 (0.85%)
Pancreatitis acute [A] †	1/121 (0.83%)	0/118 (0%)
Small intestinal obstruction [A] †	1/121 (0.83%)	0/118 (0%)
General disorders		
Hernia [A] †	0/121 (0%)	1/118 (0.85%)
Non-cardiac chest pain [A] †	0/121 (0%)	2/118 (1.69%)
Hepatobiliary disorders		
Cholecystitis [A] †	1/121 (0.83%)	0/118 (0%)
Cholelithiasis [A] †	0/121 (0%)	1/118 (0.85%)
Infections and infestations		
Appendicitis [A] †	0/121 (0%)	1/118 (0.85%)
Enterococcal infection [A] †	1/121 (0.83%)	0/118 (0%)

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
	Affected/At Risk (%)	Affected/At Risk (%)
Escherichia bacteraemia [A] †	0/121 (0%)	1/118 (0.85%)
Gastroenteritis [A] †	1/121 (0.83%)	0/118 (0%)
Pneumonia [A] †	1/121 (0.83%)	3/118 (2.54%)
Respiratory tract infection [A] †	0/121 (0%)	1/118 (0.85%)
Injury, poisoning and procedural complications		
Spinal compression fracture [A] †	1/121 (0.83%)	0/118 (0%)
Therapeutic agent toxicity [A] [1] †	1/121 (0.83%)	0/118 (0%)
Metabolism and nutrition disorders		
Failure to thrive [A] †	1/121 (0.83%)	0/118 (0%)
Hyponatraemia [A] †	1/121 (0.83%)	0/118 (0%)
Musculoskeletal and connective tissue disorders		
Lumbar spinal stenosis [A] †	1/121 (0.83%)	0/118 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma [A] †	0/121 (0%)	1/118 (0.85%)
Metastases to liver [A] †	1/121 (0.83%)	0/118 (0%)
Nervous system disorders		
Cerebrovascular accident [A] †	0/121 (0%)	1/118 (0.85%)
Stupor [A] †	1/121 (0.83%)	0/118 (0%)
Renal and urinary disorders		
Renal failure [A] †	1/121 (0.83%)	0/118 (0%)
Respiratory, thoracic and mediastinal disorders		
Respiratory failure [A] †	1/121 (0.83%)	2/118 (1.69%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.0

[1] verbatim term= digoxin toxicity

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5.0%

	Dexamethasone and Ranibizumab	Sham and Ranibizumab
	Affected/At Risk (%)	Affected/At Risk (%)
Total	86/121 (71.07%)	59/118 (50%)
Eye disorders		
Cataract [A] †	4/121 (3.31%)	7/118 (5.93%)
Cataract subcapsular [A] †	6/121 (4.96%)	1/118 (0.85%)
Conjunctival haemorrhage [A] †	23/121 (19.01%)	12/118 (10.17%)
Eye pain [A] †	5/121 (4.13%)	8/118 (6.78%)
Intraocular pressure increased [A] †	16/121 (13.22%)	5/118 (4.24%)
Macular degeneration [A] †	6/121 (4.96%)	5/118 (4.24%)
Retinal haemorrhage [A] †	9/121 (7.44%)	7/118 (5.93%)
Visual acuity reduced [A] †	9/121 (7.44%)	5/118 (4.24%)
Vitreous detachment [A] †	2/121 (1.65%)	7/118 (5.93%)
Vitreous floaters [A] †	6/121 (4.96%)	2/118 (1.69%)

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA 10.0

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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