ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 03/13/2013

ClinicalTrials.gov ID: NCT00658619

Study Identification

Unique Protocol ID:	190342-032D
Brief Title:	Safety and Efficacy of Brimonidine Intravitreal Implant in Patients With Geographic Atrophy Due to Age-related Macular Degeneration (AMD)
Official Title:	Safety and Efficacy of Brimonidine Intravitreal Implant in Patients With Geographic Atrophy Due to AMD
Secondary IDs:	

Study Status

Record Verification:	March 2013
Overall Status:	Completed
Study Start:	May 2008
Primary Completion:	June 2010 [Actual]
Study Completion:	April 2011 [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: 70,503 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:	Stage 1 is a patient-masked, dose-escalation, safety evaluation of brimonidine intravitreal implant. Patients will receive implant in one eye and "sham" treatment (meaning no treatment) in the fellow eye. Stage 2 will begin after 1 month of safety has been evaluated for Stage 1. Stage 2 is a randomized, double-masked, dose-response, sham-controlled evaluation of the safety and efficacy of brimonidine intravitreal implant in patients with geographic atrophy from age-related macular degeneration. Patients will be followed for up to 2 years.
Detailed Description:	

Conditions

Conditions:	Macular Degeneration
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	5

Masking:	Double Blind (Subject, Caregiver, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	119 [Actual]

Arms and Interventions

Arms	Assigned Interventions
400 µg Brimonidine Tartrate Implant Stage 1 Stage 1: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.	Drug: 400 µg Brimonidine Tartrate Implant 400 µg brimonidine tartrate implant in the study eye on Day 1 and Month 6. Other Names: • Brimonidine Tartrate PS DDS® Sham (no implant) Sham in one or both eyes on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 1 Stage 1: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.	Drug: 200 µg Brimonidine Tartrate Implant 200 µg brimonidine tartrate implant in the study eye on Day 1 and Month 6. Other Names: • Brimonidine Tartrate PS DDS® Sham (no implant) Sham in one or both eyes on Day 1 and Month 6.
400 µg Brimonidine Tartrate Implant Stage 2 Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.	Drug: 400 µg Brimonidine Tartrate Implant 400 µg brimonidine tartrate implant in the study eye on Day 1 and Month 6. Other Names: • Brimonidine Tartrate PS DDS® Sham (no implant) Sham in one or both eyes on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2 Stage 2: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.	Drug: 200 µg Brimonidine Tartrate Implant 200 µg brimonidine tartrate implant in the study eye on Day 1 and Month 6. Other Names: • Brimonidine Tartrate PS DDS® Sham (no implant) Sham in one or both eyes on Day 1 and Month 6.
Sham Comparator: Sham (no implant) Stage 2 Stage 2: sham in both eyes on Day 1 and Month 6.	Sham (no implant) Sham in one or both eyes on Day 1 and Month 6.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 50 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Geographic atrophy in both eyes due to age-related macular degeneration
- Visual acuity between 20/40 to 20/320

Exclusion Criteria:

- Known allergy to brimonidine
- Uncontrolled systemic disease or infection of the eye
- Recent eye surgery or injections in the eye
- Female patients who are pregnant, nursing or planning a pregnancy

Contacts/Locations

Study Officials: Medical Director
Study Director
Allergan, Inc.

Locations: United States, Texas
Abilene, Texas, United States

Korea, Republic of
Seoul, Korea, Republic of

Australia, New South Wales
Sydney, New South Wales, Australia

Germany
Karlsruhe, Germany

Italy
Udine, Italy

Portugal
Coimbra, Portugal, Portugal

Philippines
Makati City, Philippines

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	Stage 1 of the study was a patient-masked, dose-escalation, paired-eye comparison and the Investigator was not masked. Stage 2 was a parallel-group, sham-controlled, paired-eye comparison. Investigators were masked as to dose received for patients in the active treatment groups. No patients from Stage 1 were enrolled in Stage 2.

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant Stage 1	Stage 1: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 1	Stage 1: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
400 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Overall Study

	400 µg Brimonidine Tartrate Implant Stage 1	200 µg Brimonidine Tartrate Implant Stage 1	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Started	3	3	41	49	23
Completed	3	2	31	37	21
Not Completed	0	1	10	12	2

Baseline Characteristics

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant Stage 1	Stage 1: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 1	Stage 1: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
400 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Baseline Measures

	400 µg Brimonidine Tartrate Implant Stage 1	200 µg Brimonidine Tartrate Implant Stage 1	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2	Total
Number of Participants	3	3	41	49	23	119
Age, Continuous [units: Years] Mean (Standard Deviation)	85.0 (3.61)	79.0 (3.00)	75.6 (8.78)	77.0 (9.13)	78.4 (5.80)	77.0 (8.33)
Gender, Male/Female [units: Participants]						
Female	3	2	27	28	12	72

	400 µg Brimonidine Tartrate Implant Stage 1	200 µg Brimonidine Tartrate Implant Stage 1	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2	Total
Male	0	1	14	21	11	47

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in Size of Geographic Atrophy Lesion Area in the Study Eye
Measure Description	Change from baseline in size of geographic atrophy lesion area in the study eye is based on fundus photography as read by an independent Reading Center. Photographs are taken with a specialized microscope with an attached camera to photograph the interior of the eye, including the retina and optic disc. A positive change from baseline indicates an increase in size of geographic atrophy lesion area (worsening; disease progression). Data are reported in disc area where 1 disc area = 2.54 millimeters squared (mm^2).
Time Frame	Baseline, Month 12
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: All randomized patients who participated in Stage 2

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Measured Values

	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Number of Participants Analyzed	41	49	23
Change From Baseline in Size of Geographic Atrophy Lesion Area in the Study Eye [units: Disc Area] Mean (Standard Deviation)			

	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Baseline	6.219 (3.9524)	6.897 (4.6397)	5.526 (4.7890)
Change from Baseline at Month 12	0.898 (0.7520)	1.006 (0.7858)	1.239 (1.1645)

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in Size of Geographic Atrophy Lesion Area in the Study Eye
Measure Description	Change from baseline in size of geographic atrophy lesion area in the study eye is based on fundus photography as read by an independent Reading Center. Photographs are taken with a specialized microscope with an attached camera to photograph the interior of the eye, including the retina and optic disc. A positive change from baseline indicates an increase in size of geographic atrophy lesion area (worsening; disease progression). Data are reported in disc area where 1 disc area = 2.54 millimeters squared (mm^2).
Time Frame	Baseline, Month 3, Month 6, Month 9, Month 18, Month 24
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: All randomized patients who participated in Stage 2

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 200 µg brimonidine tartrate implant in study eye and sham in fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Measured Values

	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Number of Participants Analyzed	41	49	23
Change From Baseline in Size of Geographic Atrophy Lesion Area in the Study Eye [units: Disc Area] Mean (Standard Deviation)			

	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Baseline	6.219 (3.9524)	6.897 (4.6397)	5.526 (4.7890)
Change from Baseline at Month 3	0.182 (0.3353)	0.117 (0.6612)	0.399 (0.3713)
Change from Baseline at Month 6	0.482 (0.6325)	0.570 (0.5749)	0.609 (0.5474)
Change from Baseline at Month 9	0.641 (0.6847)	0.798 (0.6424)	0.857 (0.7267)
Change from Baseline at Month 18	1.306 (1.0164)	1.413 (1.0291)	1.697 (1.4185)
Change from Baseline at Month 24	1.744 (1.4010)	1.991 (1.4469)	2.178 (1.7042)

3. Secondary Outcome Measure:

Measure Title	Change From Baseline 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) in the study eye. The lower the number of letters read correctly on the eye chart, the worse the vision (or visual acuity). A positive change from baseline indicates an improvement and a negative change from baseline indicates a worsening.
Time Frame	Baseline, 24 Months
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: All randomized patients who participated in Stage 2

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 200 µg brimonidine tartrate implant in study eye and sham in fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Measured Values

	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Number of Participants Analyzed	41	49	23
Change From Baseline in Best Corrected Visual Acuity (BCVA) in the Study Eye [units: Number of Letters Read Correctly] Mean (Standard Deviation)			
Baseline	54.8 (12.89)	52.1 (13.91)	53.7 (10.71)
Change from Baseline at 24 Months	-5.0 (13.77)	-3.2 (12.87)	-3.3 (12.98)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Contrast Sensitivity in the Study Eye
Measure Description	Change from baseline in contrast sensitivity in the study eye is measured using a Pelli-Robson contrast sensitivity chart at 1 meter. The contrast sensitivity chart contains letters that are darkest at the top and then get progressively lighter. Scores range from 0 to 48 and are based on the number of letters read correctly. A negative change from baseline indicates a worsening in contrast sensitivity and a positive change from baseline indicates an improvement.
Time Frame	Baseline, 24 Months
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: All randomized patients who participated in Stage 2

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 200 µg brimonidine tartrate implant in study eye and sham in fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Measured Values

	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Number of Participants Analyzed	41	49	23
Change From Baseline in Contrast Sensitivity in the Study Eye [units: Number of Letters Read Correctly] Mean (Standard Deviation)			
Baseline	23.7 (5.60)	22.1 (5.76)	21.7 (7.56)
Change from Baseline at 24 Months	-0.9 (4.33)	1.1 (7.22)	0.6 (7.49)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in Reading Speed in the Study Eye
Measure Description	Change from baseline in reading speed in the study eye is assessed using modified Bailey-Lovie word charts. Patients read the chart for 2 minutes and the numbers of words read correctly per minute are totaled. An increase in the number of words read correctly indicates an improvement and a decrease in the number of words read correctly indicates a worsening.
Time Frame	Baseline, 24 Months
Safety Issue?	No

Analysis Population Description

Intent-to-Treat: All randomized patients who participated in Stage 2

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant Stage 2	Stage 2: 200 µg brimonidine tartrate implant in study eye and sham in fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Measured Values

	400 µg Brimonidine Tartrate Implant Stage 2	200 µg Brimonidine Tartrate Implant Stage 2	Sham (no Implant) Stage 2
Number of Participants Analyzed	41	49	23
Change From Baseline in Reading Speed in the Study Eye [units: Words per Minute (wpm)] Mean (Standard Deviation)			
Baseline	10.21 (8.532)	9.62 (9.224)	8.72 (6.832)
Change from Baseline at 24 Months	-1.15 (5.527)	-0.28 (7.035)	0.45 (4.705)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The Safety Population was used for adverse events (AEs) and serious adverse events (SAEs) and included all patients who were enrolled and treated in the study. For Ocular AEs, only those occurring in the study eye are reported in the "Other Adverse Events" section. For SAEs, all ocular events are reported, regardless of eye.

Reporting Groups

	Description
400 µg Brimonidine Tartrate Implant	Stage 1 and 2 combined: 400 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
200 µg Brimonidine Tartrate Implant	Stage 1 and 2 combined: 200 µg brimonidine tartrate implant in the study eye and sham in the fellow eye on Day 1 and Month 6.
Sham (no Implant) Stage 2	Stage 2: sham in both eyes on Day 1 and Month 6.

Serious Adverse Events

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	14/43 (32.56%)	20/51 (39.22%)	9/23 (39.13%)
Blood and lymphatic system disorders			

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Anaemia [A] †	0/43 (0%)	1/51 (1.96%)	1/23 (4.35%)
Cardiac disorders			
Acute Myocardial Infarction [A] †	1/43 (2.33%)	1/51 (1.96%)	1/23 (4.35%)
Angina Pectoris [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Angina Unstable [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Aortic Valve Stenosis [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Atrial Fibrillation [A] †	1/43 (2.33%)	1/51 (1.96%)	1/23 (4.35%)
Atrial Flutter [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Cardiac Failure Congestive [A] †	1/43 (2.33%)	1/51 (1.96%)	0/23 (0%)
Coronary Artery Disease [A] †	1/43 (2.33%)	1/51 (1.96%)	0/23 (0%)
Mitral Valve Stenosis [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Myocardial Infarction [A] †	1/43 (2.33%)	2/51 (3.92%)	0/23 (0%)
Sick Sinus Syndrome [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Ear and labyrinth disorders			
Vertigo [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Eye disorders			
Visual Acuity Reduced [A] *	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Gastrointestinal disorders			
Abdominal Pain Lower [A] *	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Diverticulum [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Gastrointestinal Haemorrhage [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Oesophageal Stenosis [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Small Intestinal Obstruction [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Infections and infestations			
Cellulitis [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Clostridium Difficile Colitis [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Diarrhoea Infectious [A] *	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Diverticulitis [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Pneumonia [A] †	1/43 (2.33%)	1/51 (1.96%)	1/23 (4.35%)
Urinary Tract Infection Bacterial [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Urosepsis [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Injury, poisoning and procedural complications			
Femoral Neck Fracture [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Femur Fracture [A] †	0/43 (0%)	2/51 (3.92%)	0/23 (0%)
Hip Fracture [A] †	1/43 (2.33%)	1/51 (1.96%)	1/23 (4.35%)
Road Traffic Accident [A] *	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Spinal Compression Fracture [A] †	0/43 (0%)	0/51 (0%)	2/23 (8.7%)
Metabolism and nutrition disorders			
Dehydration [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Hyponatraemia [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Musculoskeletal and connective tissue disorders			
Flank Pain [A] *	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma [A] †	1/43 (2.33%)	1/51 (1.96%)	1/23 (4.35%)

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Bladder Cancer [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Bowen's Disease [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Laryngeal Cancer [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Lung Cancer Metastatic [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Lung Squamous Cell Carcinoma Stage Unspecified [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Malignant Melanoma [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Non-Hodgkin's Lymphoma [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Small Cell Lung Cancer Stage Unspecified [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Squamous Cell Carcinoma [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Transitional Cell Carcinoma [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Nervous system disorders			
Carotid Artery Stenosis [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Cerebrovascular Accident [A] †	1/43 (2.33%)	2/51 (3.92%)	0/23 (0%)
Dizziness [A] *	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Intracranial Aneurysm [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Syncope [A] *	1/43 (2.33%)	0/51 (0%)	1/23 (4.35%)
Transient Ischaemic Attack [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Renal and urinary disorders			
Haematuria [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Nephrolithiasis [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Renal Failure [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Renal Failure Acute [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Stress Urinary Incontinence [A] *	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Urinary Retention [A] *	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)
Pulmonary Vascular Disorder [A] †	1/43 (2.33%)	0/51 (0%)	0/23 (0%)
Respiratory Failure [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Vascular disorders			
Aortic Stenosis [A] †	0/43 (0%)	1/51 (1.96%)	0/23 (0%)
Hypotension [A] †	0/43 (0%)	0/51 (0%)	1/23 (4.35%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA version 10.0

Other Adverse Events

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

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	38/43 (88.37%)	47/51 (92.16%)	20/23 (86.96%)
Blood and lymphatic system disorders			
Anaemia [A] †	1/43 (2.33%)	5/51 (9.8%)	3/23 (13.04%)
Leukocytosis [A] †	0/43 (0%)	3/51 (5.88%)	0/23 (0%)
Cardiac disorders			
Angina pectoris [A] †	0/43 (0%)	3/51 (5.88%)	1/23 (4.35%)

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Coronary Artery Disease [A] †	1/43 (2.33%)	2/51 (3.92%)	2/23 (8.7%)
Endocrine disorders			
Hypothyroidism [A] †	0/43 (0%)	1/51 (1.96%)	2/23 (8.7%)
Eye disorders			
Cataract [A] †	4/43 (9.3%)	3/51 (5.88%)	1/23 (4.35%)
Conjunctival Haemorrhage [A] †	12/43 (27.91%)	21/51 (41.18%)	2/23 (8.7%)
Conjunctival Hyperaemia [A] †	3/43 (6.98%)	7/51 (13.73%)	3/23 (13.04%)
Eye Pain [A] *	5/43 (11.63%)	1/51 (1.96%)	1/23 (4.35%)
Posterior Capsule Opacification [A] †	3/43 (6.98%)	0/51 (0%)	0/23 (0%)
Punctate Keratitis [A] †	5/43 (11.63%)	1/51 (1.96%)	0/23 (0%)
Retinal Haemorrhage [A] †	3/43 (6.98%)	3/51 (5.88%)	2/23 (8.7%)
Visual Acuity Reduced [A] *	3/43 (6.98%)	3/51 (5.88%)	0/23 (0%)
Vitreous Detachment [A] †	2/43 (4.65%)	1/51 (1.96%)	2/23 (8.7%)
Vitreous Floaters [A] *	3/43 (6.98%)	2/51 (3.92%)	0/23 (0%)
Vitreous Haemorrhage [A] †	2/43 (4.65%)	3/51 (5.88%)	0/23 (0%)
Gastrointestinal disorders			
Constipation [A] *	0/43 (0%)	3/51 (5.88%)	2/23 (8.7%)
Dental Caries [A] †	0/43 (0%)	0/51 (0%)	2/23 (8.7%)
Nausea [A] *	0/43 (0%)	3/51 (5.88%)	3/23 (13.04%)
Infections and infestations			
Ear Infection [A] †	1/43 (2.33%)	2/51 (3.92%)	2/23 (8.7%)
Pneumonia [A] †	1/43 (2.33%)	3/51 (5.88%)	1/23 (4.35%)

	400 µg Brimonidine Tartrate Implant	200 µg Brimonidine Tartrate Implant	Sham (no Implant) Stage 2
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Sinusitis [A] †	4/43 (9.3%)	0/51 (0%)	1/23 (4.35%)
Urinary Tract Infection [A] †	3/43 (6.98%)	5/51 (9.8%)	2/23 (8.7%)
Injury, poisoning and procedural complications			
Fall [A] *	1/43 (2.33%)	3/51 (5.88%)	1/23 (4.35%)
Spinal Compression Fracture [A] †	0/43 (0%)	0/51 (0%)	2/23 (8.7%)
Musculoskeletal and connective tissue disorders			
Arthralgia [A] *	0/43 (0%)	3/51 (5.88%)	1/23 (4.35%)
Back Pain [A] *	1/43 (2.33%)	0/51 (0%)	3/23 (13.04%)
Nervous system disorders			
Cerebrovascular Accident [A] †	1/43 (2.33%)	3/51 (5.88%)	0/23 (0%)
Syncope [A] *	3/43 (6.98%)	1/51 (1.96%)	2/23 (8.7%)
Renal and urinary disorders			
Nephrolithiasis [A] †	0/43 (0%)	0/51 (0%)	2/23 (8.7%)
Respiratory, thoracic and mediastinal disorders			
Sleep Apnoea Syndrome [A] †	0/43 (0%)	0/51 (0%)	2/23 (8.7%)
Skin and subcutaneous tissue disorders			
Urticaria [A] *	0/43 (0%)	0/51 (0%)	2/23 (8.7%)
Vascular disorders			
Hypertension [A] †	2/43 (4.65%)	1/51 (1.96%)	4/23 (17.39%)

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

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