Clinical trial results:
A Multicenter, Patient-Masked, Safety Extension Study to Evaluate the Biodegradation of the Brimonidine Tartrate Posterior Segment Drug Delivery System

Summary

EudraCT number	2010-019079-32
Trial protocol	PT DE GB CZ IT
Global end of trial date	05 February 2014

Results information

Result version number	v1 (current)
This version publication date	07 January 2017
First version publication date	07 January 2017

Trial information

Trial identification

Sponsor protocol code	190342-033D

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01080209
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan Limited
Sponsor organisation address	Allergan Limited Marlow International The Parkway, Marlow, United Kingdom, SL7 1YL
Public contact	Allergan Limited EU Regulatory Dept, Allergan Limited, 44 1628 494444, ml-eu_reg_affairs@allergan.com
Scientific contact	Allergan Limited EU Regulatory Dept, Allergan Limited, 44 1628 494444, ml-eu_reg_affairs@allergan.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2014
Global end of trial reached?	Yes
Global end of trial date	05 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the biodegradation and related safety profile of the intravitreal Brimonidine Tartrate Posterior Segment Drug Delivery System (Brimonidine Tartrate PS DDS®) implant matrix

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 142
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Czech Republic: 9
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	India: 2
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Philippines: 10
Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Korea, Republic of: 4
Worldwide total number of subjects	215
EEA total number of subjects	47

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	71
From 65 to 84 years	121
85 years and over	23

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients enrolled in this extension study from the following parent studies: 190342-027D, 190342-028D, 190342-030D, 190342-031D, 190342-032D, and 190342-036. No treatment was administered in this study, so the treatment groups reflect the treatments received in the parent studies.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Brimo PS DDS® 400 µg (2 implants)

Arm description:

Patients who received Brimo PS DDS® 400 µg (2 implants) in a previous study.

Arm type	Experimental
Investigational medicinal product name	Brimo PS DDS®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use

Dosage and administration details:

Patients who received Brimo PS DDS® 400 µg (2 implants) in a previous study.

Arm title	Brimo PS DDS® 400 µg (1 implant)

Arm description:

Patients who received Brimo PS DDS® 400 µg (1 implant) in a previous study.

Arm type	Experimental
Investigational medicinal product name	Brimo PS DDS®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use

Dosage and administration details:

Patients who received Brimo PS DDS® 400 µg (1 implant) in a previous study.

Arm title	Brimo PS DDS® 200 µg (2 implants)

Arm description:

Patients who received Brimo PS DDS® 200 µg (2 implants) in a previous study.

Arm type	Experimental
Investigational medicinal product name	Brimo PS DDS®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use

Dosage and administration details:
Patients who received Brimo PS DDS® 200 µg (2 implants) in a previous study.

Arm title	Brimo PS DDS® 200 µg (1 implant)
Arm description:	
Patients who received Brimo PS DDS® 200 µg (1 implant) in a previous study.	
Arm type	Experimental
Investigational medicinal product name	Brimo PS DDS®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use
Dosage and administration details:	
Patients who received Brimo PS DDS® 200 µg (1 implant) in a previous study.	
Arm title	Brimo PS DDS® 100 µg (1 implant)
Arm description:	
Patients who received Brimo PS DDS® 100 µg (1 implant) in a previous study.	
Arm type	Experimental
Investigational medicinal product name	Brimo PS DDS®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use
Dosage and administration details:	
Patients who received Brimo PS DDS® 100 µg (1 implant) in a previous study.	
Arm title	Brimo PS DDS® 50 µg (1 implant)
Arm description:	
Patients who received Brimo PS DDS® 50 µg (1 implant) in a previous study.	
Arm type	Experimental
Investigational medicinal product name	Brimo PS DDS®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use
Dosage and administration details:	
Patients who received Brimo PS DDS® 50 µg (1 implant) in a previous study.	
Arm title	Sham
Arm description:	
Patients who received sham in a previous study.	
Arm type	Sham Procedure
Investigational medicinal product name	Sham
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Intravitreal use
Dosage and administration details:	
Patients who received sham in a previous study.	

Number of subjects in period 1	Brimo PS DDS® 400 µg (2 implants)	Brimo PS DDS® 400 µg (1 implant)	Brimo PS DDS® 200 µg (2 implants)
Started	28	53	33
Completed	22	42	28
Not completed	6	11	5
Adverse event, serious fatal	4	1	1
Adverse event, non-fatal	-	-	-
Personal Reasons	2	5	4
Principal Investigator Left Site	-	4	-
Lost to follow-up	-	1	-

Number of subjects in period 1	Brimo PS DDS® 200 µg (1 implant)	Brimo PS DDS® 100 µg (1 implant)	Brimo PS DDS® 50 µg (1 implant)
Started	42	6	2
Completed	37	6	2
Not completed	5	0	0
Adverse event, serious fatal	-	-	-
Adverse event, non-fatal	-	-	-
Personal Reasons	-	-	-
Principal Investigator Left Site	5	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Sham
Started	51
Completed	44
Not completed	7
Adverse event, serious fatal	2
Adverse event, non-fatal	2
Personal Reasons	1
Principal Investigator Left Site	-
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Brimo PS DDS® 400 µg (2 implants)
Reporting group description:	
Patients who received Brimo PS DDS® 400 µg (2 implants) in a previous study.	
Reporting group title	Brimo PS DDS® 400 µg (1 implant)
Reporting group description:	
Patients who received Brimo PS DDS® 400 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 200 µg (2 implants)
Reporting group description:	
Patients who received Brimo PS DDS® 200 µg (2 implants) in a previous study.	
Reporting group title	Brimo PS DDS® 200 µg (1 implant)
Reporting group description:	
Patients who received Brimo PS DDS® 200 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 100 µg (1 implant)
Reporting group description:	
Patients who received Brimo PS DDS® 100 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 50 µg (1 implant)
Reporting group description:	
Patients who received Brimo PS DDS® 50 µg (1 implant) in a previous study.	
Reporting group title	Sham
Reporting group description:	
Patients who received sham in a previous study.	

Reporting group values	Brimo PS DDS® 400 µg (2 implants)	Brimo PS DDS® 400 µg (1 implant)	Brimo PS DDS® 200 µg (2 implants)
Number of subjects	28	53	33
Age categorical Units: Subjects			
Adults (18-64 years)	2	23	3
From 65-84 years	19	29	24
85 years and over	7	1	6
Age continuous Units: years			
arithmetic mean	77.7	63	78
standard deviation	± 8.75	± 15.32	± 8.47
Gender, Male/Female Units: Participants			
Female	19	24	17
Male	9	29	16

Reporting group values	Brimo PS DDS® 200 µg (1 implant)	Brimo PS DDS® 100 µg (1 implant)	Brimo PS DDS® 50 µg (1 implant)
Number of subjects	42	6	2
Age categorical Units: Subjects			
Adults (18-64 years)	20	3	0
From 65-84 years	19	3	1
85 years and over	3	0	1

Age continuous Units: years			
arithmetic mean	63.3	60.8	78
standard deviation	± 15.05	± 11.91	± 9.9
Gender, Male/Female Units: Participants			
Female	20	3	2
Male	22	3	0

Reporting group values	Sham	Total	
Number of subjects	51	215	
Age categorical Units: Subjects			
Adults (18-64 years)	20	71	
From 65-84 years	26	121	
85 years and over	5	23	
Age continuous Units: years			
arithmetic mean	68.2		
standard deviation	± 14.17	-	
Gender, Male/Female Units: Participants			
Female	21	106	
Male	30	109	

End points

End points reporting groups

Reporting group title	Brimo PS DDS® 400 µg (2 implants)
Reporting group description: Patients who received Brimo PS DDS® 400 µg (2 implants) in a previous study.	
Reporting group title	Brimo PS DDS® 400 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 400 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 200 µg (2 implants)
Reporting group description: Patients who received Brimo PS DDS® 200 µg (2 implants) in a previous study.	
Reporting group title	Brimo PS DDS® 200 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 200 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 100 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 100 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 50 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 50 µg (1 implant) in a previous study.	
Reporting group title	Sham
Reporting group description: Patients who received sham in a previous study.	

Primary: Number of Patients with No Visible Implants in the Study Eye

End point title	Number of Patients with No Visible Implants in the Study Eye[1]
End point description: Implants administered during the parent study are evaluated during this study to determine if they have completely degraded. The time frame is evaluated from the point of the first treatment in the parent study.	
End point type	Primary
End point timeframe: Month 36	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analyses for this end point.

End point values	Brimo PS DDS® 400 µg (2 implants)	Brimo PS DDS® 400 µg (1 implant)	Brimo PS DDS® 200 µg (2 implants)	Brimo PS DDS® 200 µg (1 implant)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	42	30	37
Units: Patients	14	37	26	35

End point values	Brimo PS	Brimo PS	Sham	

	DDS® 100 µg (1 implant)	DDS® 50 µg (1 implant)		
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	2	46	
Units: Patients	6	2	46	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients with Vision Loss in the Study Eye

End point title	Number of Patients with Vision Loss in the Study Eye

End point description:

Vision loss is assessed by Best Corrected Visual Acuity (BCVA) in the study eye. 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). Severe vision loss is a ≥30 letter decrease in BCVA. Moderate vision loss is a ≥15 and <30 letter decrease in BCVA. No or mild vision loss is <15 letter decrease in BCVA. Baseline of the parent study is defined as the point of the first study treatment.

End point type	Secondary

End point timeframe:

Baseline of Parent Study, Month 36

End point values	Brimo PS DDS® 400 µg (2 implants)	Brimo PS DDS® 400 µg (1 implant)	Brimo PS DDS® 200 µg (2 implants)	Brimo PS DDS® 200 µg (1 implant)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	42	30	37
Units: Patients				
Severe Vision Loss	3	1	1	0
Moderate Vision Loss	6	0	6	1
No or Mild Vision Loss	14	41	23	36

End point values	Brimo PS DDS® 100 µg (1 implant)	Brimo PS DDS® 50 µg (1 implant)	Sham	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	2	46	
Units: Patients				
Severe Vision Loss	0	0	4	
Moderate Vision Loss	0	0	6	
No or Mild Vision Loss	6	2	36	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events were monitored from informed consent signature to the end of study for each subject.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Brimo PS DDS® 400 µg (2 implants)
Reporting group description: Patients who received Brimo PS DDS® 400 µg (2 implants) in a previous study.	
Reporting group title	Brimo PS DDS® 400 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 400 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 200 µg (2 implants)
Reporting group description: Patients who received Brimo PS DDS® 200 µg (2 implants) in a previous study.	
Reporting group title	Brimo PS DDS® 200 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 200 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 100 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 100 µg (1 implant) in a previous study.	
Reporting group title	Brimo PS DDS® 50 µg (1 implant)
Reporting group description: Patients who received Brimo PS DDS® 50 µg (1 implant) in a previous study.	
Reporting group title	Sham
Reporting group description: Patients who received sham in a previous study.	

Serious adverse events	Brimo PS DDS® 400 µg (2 implants)	Brimo PS DDS® 400 µg (1 implant)	Brimo PS DDS® 200 µg (2 implants)
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 28 (28.57%)	11 / 53 (20.75%)	7 / 33 (21.21%)
number of deaths (all causes)	4	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Cancer			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lung Cancer Metastatic			

subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lung Neoplasm Malignant			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Adenocarcinoma			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's Lymphoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular Carcinoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate Cancer	Additional description: Males Only		
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cancer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate Cancer Recurrent	Additional description: Males Only		
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal Cell Carcinoma			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer Metastatic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal Cancer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Carcinoma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Artery Stenosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Ischaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Vascular Disorder			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intermittent Claudication			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden Cardiac Death			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Reproductive system and breast disorders			
Cystocele	Additional description: Females Only		
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectocele	Additional description: Females Only		
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign Prostatic Hyperplasia	Additional description: Males Only		
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea Exertional			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Toxicity to Various Agents			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Compression Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial Bones Fracture			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Limb Fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 28 (3.57%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Angina Pectoris			
subjects affected / exposed	1 / 28 (3.57%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular Block Second Degree			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory Arrest			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Palpitations			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myocardial Infarction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial Infarction			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Syncope			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic Stroke			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Age-Related Macular Degeneration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual Acuity Reduced			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Detachment			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Vein Occlusion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anterior Chamber Inflammation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open Angle Glaucoma			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic Atrophy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocele			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis Ulcerative			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 28 (3.57%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Spinal Stenosis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary Tract Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 53 (1.89%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Brimo PS DDS® 200 µg (1 implant)	Brimo PS DDS® 100 µg (1 implant)	Brimo PS DDS® 50 µg (1 implant)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 42 (16.67%)	2 / 6 (33.33%)	0 / 2 (0.00%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Cancer			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Cancer Metastatic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Neoplasm Malignant			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Adenocarcinoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's Lymphoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular Carcinoma			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate Cancer	Additional description: Males Only		
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cancer			

subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate Cancer Recurrent	Additional description: Males Only		
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal Cell Carcinoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast Cancer Metastatic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal Cancer			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal Carcinoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Artery Stenosis			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Ischaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral Vascular Disorder			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intermittent Claudication			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden Cardiac Death			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cystocele	Additional description: Females Only		
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rectocele	Additional description: Females Only		
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign Prostatic Hyperplasia	Additional description: Males Only		
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea Exertional			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Toxicity to Various Agents			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Compression Fracture			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial Bones Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Limb Fracture			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur Fracture			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina Pectoris			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular Block Second Degree			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory Arrest			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Myocardial Infarction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary Artery Disease			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Myocardial Infarction			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic Stroke			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Age-Related Macular Degeneration			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual Acuity Reduced			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Detachment			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Vein Occlusion			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anterior Chamber Inflammation			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open Angle Glaucoma			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Optic Atrophy			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocele			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis Ulcerative			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar Spinal Stenosis			
subjects affected / exposed	1 / 42 (2.38%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Sham		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 51 (31.37%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Cancer			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung Cancer Metastatic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung Neoplasm Malignant			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal Adenocarcinoma			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-Hodgkin's Lymphoma			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatocellular Carcinoma			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Prostate Cancer	Additional description: Males Only		
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Cancer			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate Cancer Recurrent	Additional description: Males Only		
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal Cell Carcinoma			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast Cancer Metastatic			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colorectal Cancer			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Oesophageal Carcinoma			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			

Deep Vein Thrombosis				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral Artery Stenosis				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral Ischaemia				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral Vascular Disorder				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intermittent Claudication				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Death				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden Cardiac Death				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Reproductive system and breast disorders			
Cystocele	Additional description: Females Only		
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectocele	Additional description: Females Only		
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign Prostatic Hyperplasia	Additional description: Males Only		
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea Exertional			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Toxicity to Various Agents			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip Fracture			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus Fracture			

subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal Compression Fracture				
subjects affected / exposed	2 / 51 (3.92%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Ankle Fracture				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial Bones Fracture				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Fall				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaw Fracture				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pubis Fracture				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tibia Fracture				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper Limb Fracture				

subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur Fracture				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial Fibrillation				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina Pectoris				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular Block Second Degree				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory Arrest				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute Myocardial Infarction				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Coronary Artery Disease				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial Infarction				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular Accident				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic Stroke				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Age-Related Macular Degeneration				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Visual Acuity Reduced				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal Detachment				

subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal Vein Occlusion				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anterior Chamber Inflammation				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Open Angle Glaucoma				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Optic Atrophy				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Enterocele				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis Ulcerative				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholelithiasis				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Nephrolithiasis				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Intervertebral Disc Protrusion				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar Spinal Stenosis				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 51 (1.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Clostridium Difficile Colitis				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gangrene				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection				

subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic Ketoacidosis			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Brimo PS DDS® 400 µg (2 implants)	Brimo PS DDS® 400 µg (1 implant)	Brimo PS DDS® 200 µg (2 implants)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 28 (64.29%)	40 / 53 (75.47%)	26 / 33 (78.79%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	3 / 53 (5.66%)	3 / 33 (9.09%)
occurrences (all)	0	3	3
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia	Additional description: Males Only		
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Investigations			
Intraocular Pressure Increased			
subjects affected / exposed	0 / 28 (0.00%)	6 / 53 (11.32%)	0 / 33 (0.00%)
occurrences (all)	0	8	0
Cardiac disorders			
Coronary Artery Disease			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Bradycardia			

subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Acute Coronary Syndrome			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Neuropathy Peripheral			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	3 / 33 (9.09%)
occurrences (all)	2	0	3
Dementia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Restless Legs Syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Ear Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	3 / 28 (10.71%)	6 / 53 (11.32%)	0 / 33 (0.00%)
occurrences (all)	4	9	0
Visual Acuity Reduced			
alternative assessment type: Non-systematic			

subjects affected / exposed	3 / 28 (10.71%)	3 / 53 (5.66%)	3 / 33 (9.09%)
occurrences (all)	3	4	6
Age-Related Macular Degeneration			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	3 / 33 (9.09%)
occurrences (all)	3	0	4
Vitreous Detachment			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	2 / 33 (6.06%)
occurrences (all)	4	0	2
Vitreous Floaters			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	5 / 53 (9.43%)	3 / 33 (9.09%)
occurrences (all)	0	7	4
Retinal Haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	3
Posterior Capsule Opacification			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Dry Eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	5 / 53 (9.43%)	2 / 33 (6.06%)
occurrences (all)	0	9	4
Macular Fibrosis			
subjects affected / exposed	0 / 28 (0.00%)	4 / 53 (7.55%)	0 / 33 (0.00%)
occurrences (all)	0	4	0
Optic Disc Haemorrhage			
subjects affected / exposed	0 / 28 (0.00%)	3 / 53 (5.66%)	2 / 33 (6.06%)
occurrences (all)	0	3	2
Glaucoma			
subjects affected / exposed	0 / 28 (0.00%)	3 / 53 (5.66%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
Macular Degeneration			
subjects affected / exposed	0 / 28 (0.00%)	3 / 53 (5.66%)	0 / 33 (0.00%)
occurrences (all)	0	5	0
Blepharitis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	4
Glare			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Cataract Cortical			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Cataract Subscapular			
subjects affected / exposed	0 / 28 (0.00%)	4 / 53 (7.55%)	0 / 33 (0.00%)
occurrences (all)	0	5	0
Gastrointestinal disorders			
Constipation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Gastrooesophageal Reflux Disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Dental Caries			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Stress Urinary Incontinence			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 28 (7.14%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Back Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 28 (0.00%)	3 / 53 (5.66%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
Urinary Tract Infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	3 / 53 (5.66%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Otitis Media Chronic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Diabetes Mellitus Inadequate Control			
subjects affected / exposed	0 / 28 (0.00%)	0 / 53 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Brimo PS DDS® 200 µg (1 implant)	Brimo PS DDS® 100 µg (1 implant)	Brimo PS DDS® 50 µg (1 implant)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 42 (83.33%)	4 / 6 (66.67%)	2 / 2 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia	Additional description: Males Only		
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Investigations			
Intraocular Pressure Increased			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	7	0	0
Cardiac disorders			
Coronary Artery Disease			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Acute Coronary Syndrome			

subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Neuropathy Peripheral			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dementia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Restless Legs Syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	6 / 42 (14.29%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	8	0	0
Visual Acuity Reduced			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 42 (11.90%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	8	0	0
Age-Related Macular Degeneration			

subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vitreous Detachment			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Vitreous Floaters			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Retinal Haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Posterior Capsule Opacification			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dry Eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	6	0	0
Macular Fibrosis			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Optic Disc Haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Glaucoma			
subjects affected / exposed	4 / 42 (9.52%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Macular Degeneration			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blepharitis			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Glare			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Cataract Cortical			
subjects affected / exposed	3 / 42 (7.14%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Cataract Subscapular			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal Reflux Disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dental Caries			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

Stress Urinary Incontinence			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Back Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Urinary Tract Infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Otitis Media Chronic			
subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			

subjects affected / exposed	0 / 42 (0.00%)	1 / 6 (16.67%)	2 / 2 (100.00%)
occurrences (all)	0	1	2
Gout			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Diabetes Mellitus Inadequate Control			
subjects affected / exposed	0 / 42 (0.00%)	0 / 6 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Sham		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 51 (80.39%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	4		
Reproductive system and breast disorders			
Benign Prostatic Hyperplasia	Additional description: Males Only		
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Investigations			
Intraocular Pressure Increased			
subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	8		
Cardiac disorders			
Coronary Artery Disease			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Bradycardia			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Acute Coronary Syndrome			

subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Neuropathy Peripheral			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Dementia			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Restless Legs Syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Ear Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Eye disorders			
Cataract			
subjects affected / exposed	6 / 51 (11.76%)		
occurrences (all)	11		
Visual Acuity Reduced			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Age-Related Macular Degeneration			

subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Vitreous Detachment				
subjects affected / exposed	4 / 51 (7.84%)			
occurrences (all)	6			
Vitreous Floaters				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Retinal Haemorrhage				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Posterior Capsule Opacification				
subjects affected / exposed	4 / 51 (7.84%)			
occurrences (all)	4			
Dry Eye				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Macular Fibrosis				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Optic Disc Haemorrhage				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Glaucoma				
subjects affected / exposed	5 / 51 (9.80%)			
occurrences (all)	7			
Macular Degeneration				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Blepharitis				
subjects affected / exposed	0 / 51 (0.00%)			
occurrences (all)	0			
Glare				

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Cataract Cortical			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Cataract Subscapular			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Constipation			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	3		
Dysphagia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Gastrooesophageal Reflux Disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Dental Caries			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			

Stress Urinary Incontinence alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	 0 / 51 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 0 / 51 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back Pain alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	 0 / 51 (0.00%) 0 3 / 51 (5.88%) 3		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary Tract Infection subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all) Influenza alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Otitis Media Chronic subjects affected / exposed occurrences (all)	 0 / 51 (0.00%) 0 0 / 51 (0.00%) 0 0 / 51 (0.00%) 0 0 / 51 (0.00%) 0 0 / 51 (0.00%) 0		
Metabolism and nutrition disorders Hypercholesterolaemia			

subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		
Diabetes Mellitus Inadequate Control			
subjects affected / exposed	0 / 51 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2010	1) Ensure the study design could accommodate inclusion of patients from planned and future clinical studies with Brimonidine Tartrate PS DDS; 2) Update the method of IOP measurement to one considered more suitable for assessing safety in ocular posterior segment diseases; 3) Clarify that any abortion (spontaneous or nonspontaneous) is a serious adverse event; 4) The planned number of patients was changed from 290 to approximately 300.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported