Clinical trial results:
Study of the efficacy and tolerance of intra-prostatic injection of botulinum toxin A in men for the treatment of symptomatic benign prostate hyperplasia.

Summary

EudraCT number	2010-022255-37
Trial protocol	FR
Global end of trial date	28 April 2015

Results information

Result version number	v1 (current)
This version publication date	15 January 2022
First version publication date	15 January 2022

Trial information

Trial identification

Sponsor protocol code	CHUBX2010/39

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01275521
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de Bordeaux
Sponsor organisation address	12 rue Dubernat, Talence, France, 33404
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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	21 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 April 2015
Global end of trial reached?	Yes
Global end of trial date	28 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of intra-prostatic injection of BONT-A in men in the treatment of symptomatic BPH.

Protection of trial subjects:

If an adverse event or a tolerance problem related to intra-prostatic injection of BONT-A occurs outside of the scheduled dates for follow-up visits, patients may consult an investigator at one of the investigating centres.
These emergency consultations will be conducted in the urology department during the hours of consultation or through the out-of-hours emergency department.
These consultations will be conducted to the best of the current state of medical knowledge: depending on the patient's condition, all clinical and complementary examinations necessary to take the patient's in charge may be prescribed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 127
Worldwide total number of subjects	127
EEA total number of subjects	127

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	55
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Date of first inclusion: 10-jan-2011
End date of last included patient: 28-Apr-2015
9 centres (Part of the Committee for Male Mictional Disorders of the French Association of Urology (CTMH-AFU)) in France participated in the study.

Pre-assignment

Screening details:

· Patient aged 50 to 85
· Obstructive or irritative urinary symptomatology linked to a BPH
· Score IPSS moderate to severe (8-19: moderate; 20-35: severe) or IPSS ≤ 7 in patient medically treated for symptomatic BPH
· Increase in prostate volume on the rectal touch or ultrasound
· Free consent

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	BONT-A intra-prostatic injection

Arm description:

Intra-prostatic injection of botulinum toxin A

Arm type	Experimental
Investigational medicinal product name	Botulinum toxin A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal capsule
Routes of administration	Intraprostatic use

Dosage and administration details:

Single dose of ofloxacin 200mg (or ceftriaxone 1g case of allergy) in accordance with the current recommendations concerning biospsies prostate.
Intra-prostatic injection of 200 IU BONT-A (to be diluted in 10 cc of isotonic saline), divided into 4 injection sites, 2 in each prostatic lobe, respectively 2.5 cc each.

Arm title	Optimized medical BPH treatment

Arm description:

Optimized medical BPH treatment

Arm type	Active comparator
Investigational medicinal product name	Other
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

This medical treatment can include the prescription of herbal medicine, alpha-blocker, 5 alpha reductase inhibitor, or combination of alpha-blocker and 5-alpha reductase inhibitor.

Number of subjects in period 1	BONT-A intra-prostatic injection	Optimized medical BPH treatment
Started	64	63
Completed	45	46
Not completed	19	17
Consent withdrawn by subject	16	12
Other reasons	2	4
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	BONT-A intra-prostatic injection
Reporting group description:	
Intra-prostatic injection of botulinum toxin A	
Reporting group title	Optimized medical BPH treatment
Reporting group description:	
Optimized medical BPH treatment	

Reporting group values	BONT-A intra-prostatic injection	Optimized medical BPH treatment	Total
Number of subjects	64	63	127
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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 65-84 years			55
85 years and over			1
Age continuous			
Units: years			
arithmetic mean	65.2	64.3	
standard deviation	± 7.3	± 7.6	-
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	64	63	127

Subject analysis sets	
Subject analysis set title	Per protocol BONT-A intra-prostatic injection
Subject analysis set type	Per protocol
Subject analysis set description:	
Population analysed under treatment	
Subject analysis set title	Per protocol Optimized medical BPH treatment
Subject analysis set type	Per protocol
Subject analysis set description:	
Population analysed under treatment	
Subject analysis set title	Intention-to-treat BONT-A intra-prostatic injection
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Population analysed by intention-to-treat	
Subject analysis set title	Intention-to-treat Optimized medical BPH treatment

Subject analysis set type	Intention-to-treat

Subject analysis set description:

Population analysed in intention-to-treat

Reporting group values	Per protocol BONT-A intra-prostatic injection	Per protocol Optimized medical BPH treatment	Intention-to-treat BONT-A intra-prostatic injection
Number of subjects	44	60	64
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	65.2	64.3	65.2
standard deviation	± 7.3	± 7.6	± 7.3
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	44	60	64

Reporting group values	Intention-to-treat Optimized medical BPH treatment		
Number of subjects	63		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	64.3		
standard deviation	± 7.6		
Gender categorical			
Units: Subjects			
Female	0		

Male	63		

End points

End points reporting groups

Reporting group title	BONT-A intra-prostatic injection
Reporting group description: Intra-prostatic injection of botulinum toxin A	
Reporting group title	Optimized medical BPH treatment
Reporting group description: Optimized medical BPH treatment	
Subject analysis set title	Per protocol BONT-A intra-prostatic injection
Subject analysis set type	Per protocol
Subject analysis set description: Population analysed under treatment	
Subject analysis set title	Per protocol Optimized medical BPH treatment
Subject analysis set type	Per protocol
Subject analysis set description: Population analysed under treatment	
Subject analysis set title	Intention-to-treat BONT-A intra-prostatic injection
Subject analysis set type	Intention-to-treat
Subject analysis set description: Population analysed by intention-to-treat	
Subject analysis set title	Intention-to-treat Optimized medical BPH treatment
Subject analysis set type	Intention-to-treat
Subject analysis set description: Population analysed in intention-to-treat	

Primary: Evaluation of the patient with auto-questionnaire IPSS urinary symptomatology: questions 1 to 7 (0 to 35 score)

End point title	Evaluation of the patient with auto-questionnaire IPSS urinary symptomatology: questions 1 to 7 (0 to 35 score)
End point description: Evaluation of the patient's urinary symptomatology by Internation Prostate Symptom Score (IPSS) self-assessment questionnaire with questions 1-7 assessing obstructive and irritative symptoms related to BPH (8-19 moderate, 20-35 severe)	
End point type	Primary
End point timeframe: At 4 months after the study inclusion	

End point values	Per protocol BONT-A intra-prostatic injection	Per protocol Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	60		
Units: score				
arithmetic mean (standard deviation)	12.3 (± 7.4)	12.0 (± 6.9)		

Statistical analyses

Statistical analysis title	Difference in mean IPSS score [0-35]

Statistical analysis description:

The analysis use the multiple imputation strategy with adjustment for exposure to 5 alpha-reductase inhibitor (ARI) treatment and IPSS score at M0

Comparison groups	Per protocol Optimized medical BPH treatment v Per protocol BONT-A intra-prostatic injection
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.14
upper limit	2.11

Secondary: IPSS question 8 (score 0 to 6)

End point title	IPSS question 8 (score 0 to 6)

End point description:

End point type	Secondary

End point timeframe:

At 4 months.

End point values	Intention-to-treat BONT-A intra-prostatic injection	Intention-to-treat Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	53		
Units: scores				
arithmetic mean (standard deviation)	3.1 (± 1.4)	3.1 (± 1.4)		

Statistical analyses

Statistical analysis title	Treatment effect allocated by randomisation

Statistical analysis description:

Results of the intention-to-treat analysis of the IPSS score at question 8 at M4, with adjustment for the stratification variable of randomisation and the IPSS score at question 8 at M0

Comparison groups	Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0658
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	0.03

Secondary: Measurement of urine flowmetry Qmax

End point title	Measurement of urine flowmetry Qmax
End point description:	
This endpoint is analysed only in patients with a urine volume ≥ 80mL at visit M4	
End point type	Secondary
End point timeframe:	
At 4 months	

End point values	Intention-to-treat BONT-A intra-prostatic injection	Intention-to-treat Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46	41		
Units: millilitre(s)/seconds				
arithmetic mean (standard deviation)	12.9 (± 8.2)	12.2 (± 6.0)		

Statistical analyses

Statistical analysis title	Treatment effect allocated by randomisation
Statistical analysis description:	
Results of intention-to-treat analysis of Qmax (in mL/s) at M4, with adjustment for the stratification variable of randomisation and Qmax measurement at M0	
Comparison groups	Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4529
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	1.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.66
upper limit	3.69

Secondary: Measurement of post-void residual

End point title	Measurement of post-void residual
End point description:	
Measurement of post-void residual assessed by suprapubic ultrasound or urinary catheterization evacuator	
End point type	Secondary
End point timeframe:	
At 4 months	

End point values	Intention-to-treat BONT-A intra-prostatic injection	Intention-to-treat Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54	52		
Units: millilitre(s)				
arithmetic mean (standard deviation)	59.7 (± 77.2)	70.3 (± 95.5)		

Statistical analyses

Statistical analysis title	Treatment effect allocated by randomisation
Statistical analysis description:	
Results of intention-to-treat analysis of post-void residual measurements (in mL) at M4, with adjustment for the stratification variable of randomisation	
Comparison groups	Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5207
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	-10.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.07
upper limit	22.45

Secondary: Measurement of prostate volume

End point title	Measurement of prostate volume
End point description: Measurement of prostate volume assessed by endorectal ultrasound	
End point type	Secondary
End point timeframe: At 4 months	

End point values	Intention-to-treat BONT-A intra-prostatic injection	Intention-to-treat Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	50		
Units: millilitre(s)				
arithmetic mean (standard deviation)	58.4 (± 31.4)	51.8 (± 30.2)		

Statistical analyses

Statistical analysis title	Treatment effect allocated by randomisation
Statistical analysis description: Results of intention-to-treat analysis of prostate volume measurements (in mL) at M4, with adjustment for the stratification variable of randomisation	
Comparison groups	Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2686
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	6.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.21
upper limit	18.53

Secondary: Evaluation of erectile function using the IIEF-5 self-assessment questionnaire (score from 0 to 24)

End point title	Evaluation of erectile function using the IIEF-5 self-assessment

	questionnaire (score from 0 to 24)

End point description:

Evaluation of erectile function using the International Index of Erectile Dysfunction score (IIEF-5) self-assessment questionnaire (score from 0 to 24)

End point type	Secondary

End point timeframe:

At 4 months

End point values	Intention-to-treat BONT-A intra-prostatic injection	Intention-to-treat Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	53		
Units: scores				
arithmetic mean (standard deviation)	14.9 (± 8.3)	14.1 (± 7.7)		

Statistical analyses

Statistical analysis title	Treatment effect allocated by randomisation

Statistical analysis description:

Results of ITT analysis of IIEF-5 score at M4, with adjustment for randomisation stratification variable

Comparison groups	Intention-to-treat Optimized medical BPH treatment v Intention-to-treat BONT-A intra-prostatic injection
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5438
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.04
upper limit	3.85

Secondary: Evaluation of urinary continence by ICS 1 scores (score from 0 to 23)

End point title	Evaluation of urinary continence by ICS 1 scores (score from 0 to 23)

End point description:

Evaluation of urinary continence by Internation Continence Society Score 1 (ICS 1) (score from 0 to 23)

End point type	Secondary

End point timeframe:

At 4 months

End point values	Intention-to-treat BONT-A intra-prostatic injection	Intention-to-treat Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	53		
Units: scores				
arithmetic mean (standard deviation)	1.1 (± 2.2)	0.6 (± 1.5)		

Statistical analyses

Statistical analysis title	Treatment effect allocated by randomisation
Statistical analysis description:	
Results of intention-to-treat analysis of ICS1 score at M4, with adjustment for randomisation stratification variable and ICS1 score at M0	
Comparison groups	Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.789
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.49

Secondary: Evaluation of urinary continence by ICS 2 scores (score from 0 to 12)

End point title	Evaluation of urinary continence by ICS 2 scores (score from 0 to 12)
End point description:	
End point type	Secondary
End point timeframe:	
At 4 months	

End point values	Intention-to-treat BONT-A intra-prostatic injection	Intention-to-treat Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	53		
Units: scores				
arithmetic mean (standard deviation)	1.2 (± 2.4)	0.7 (± 1.9)		

Statistical analyses

Statistical analysis title	Effect of treatment allocated by randomisation

Statistical analysis description:

Results of intention-to-treat analysis of ICS2 score at M4, with adjustment for randomisation stratification variable and ICS2 score at M0

Comparison groups	Intention-to-treat BONT-A intra-prostatic injection v Intention-to-treat Optimized medical BPH treatment
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4458
Method	Regression, Linear
Parameter estimate	Slope
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.83

Secondary: Need for surgical intervention

End point title	Need for surgical intervention

End point description:

End point type	Secondary

End point timeframe:

At 4 months

End point values	Per protocol BONT-A intra-prostatic injection	Per protocol Optimized medical BPH treatment		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44	60		
Units: percent				
number (not applicable)				
Yes	4.5	8.3		
No	95.5	91.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall study

Adverse event reporting additional description:

These adverse events described by PT occurred during follow-up (before and after M4)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	BONT-A intra-prostatic injection

Reporting group description: -

Reporting group title	Optimized medical BPH treatment

Reporting group description: -

Serious adverse events	BONT-A intra-prostatic injection	Optimized medical BPH treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 64 (28.13%)	15 / 63 (23.81%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of prostate (10001186)	Additional description: Adenocarcinoma of prostate (10001186)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplasia (10028532)	Additional description: Myelodysplasia (10028532)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung (10041826)	Additional description: Squamous cell carcinoma of lung (10041826)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			

Critical limb ischemia (10058069)	Additional description: Critical limb ischemia (10058069)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension (10021097)	Additional description: Hypotension (10021097)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Anoplasty (10068132)	Additional description: Anoplasty (10068132)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic diet (10064725)	Additional description: Diabetic diet (10064725)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hospitalisation (10054112)	Additional description: Hospitalisation (10054112)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia hiatus repair (10019915)	Additional description: Hernia hiatus repair (10019915)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee prosthesis insertion (10050155)	Additional description: Knee prosthesis insertion (10050155)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laser prostatectomy (10023925)	Additional description: Laser prostatectomy (10023925)		
subjects affected / exposed	1 / 64 (1.56%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Prostate adenoma removal (10065313)	Additional description: Prostate adenoma removal (10065313)		
subjects affected / exposed	1 / 64 (1.56%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Removal of foreign body (10062102)	Additional description: Removal of foreign body (10062102)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toe amputation (10043913)	Additional description: Toe amputation (10043913)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral prostatectomy (10044445)	Additional description: Transurethral prostatectomy (10044445)		
subjects affected / exposed	0 / 64 (0.00%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia (10003549)	Additional description: Asthenia (10003549)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst (10011732)	Additional description: Cyst (10011732)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acute prostatitis (10001021)	Additional description: Acute prostatitis (10001021)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erection decreased (10015117)	Additional description: Erection decreased (10015117)		

subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis (10036978)	Additional description: Prostatitis (10036978)		
subjects affected / exposed	2 / 64 (3.13%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis (10015090)	Additional description: Epistaxis (10015090)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression (10012378)	Additional description: Depression (10012378)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression (10057840)	Additional description: Major depression (10057840)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Biopsy of prostate (10004825)	Additional description: Biopsy of prostate (10004825)		
subjects affected / exposed	2 / 64 (3.13%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased (10005470)	Additional description: Blood creatine phosphokinase increased (10005470)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
AFib (10001452)	Additional description: AFib (10001452)		

subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia (10047302)	Additional description: Ventricular tachycardia (10047302)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis (10007687)	Additional description: Carotid artery stenosis (10007687)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia (10016288)	Additional description: Febrile neutropenia (10016288)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia (10029354)	Additional description: Neutropenia (10029354)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye haemorrhage (10015926)	Additional description: Eye haemorrhage (10015926)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pyrosis (10037676)	Additional description: Pyrosis (10037676)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectorrhagia (10063014)	Additional description: Rectorrhagia (10063014)		

subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria (10018867)	Additional description: Haematuria (10018867)		
subjects affected / exposed	3 / 64 (4.69%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic (10038419)	Additional description: Renal colic (10038419)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention (10046555)	Additional description: Urinary retention (10046555)		
subjects affected / exposed	0 / 64 (0.00%)	2 / 63 (3.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis (10002556)	Additional description: Ankylosing spondylitis (10002556)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dupuytren's contracture (10013872)	Additional description: Dupuytren's contracture (10013872)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	BONT-A intra-prostatic injection	Optimized medical BPH treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 64 (51.56%)	28 / 63 (44.44%)	
Vascular disorders			
Essential hypertension (10015488)	Additional description: Essential hypertension (10015488)		

subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Hypotension (10021097)	Additional description: Hypotension (10021097)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Peripheral obliterative arteriopathy (10072121)	Additional description: Peripheral obliterative arteriopathy (10072121)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Bladder tumour resection (10005085)	Additional description: Bladder tumour resection (10005085)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia (10003549)	Additional description: Asthenia (10003549)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Fatigue (10016256)	Additional description: Fatigue (10016256)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Nodule (10054107)	Additional description: Nodule (10054107)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Pyrexia (10037660)	Additional description: Pyrexia (10037660)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergy (10001738)	Additional description: Allergy (10001738)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Anejaculation (10073936)	Additional description: Anejaculation (10073936)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Ejaculation failure (10014328)	Additional description: Ejaculation failure (10014328)		

subjects affected / exposed	1 / 64 (1.56%)	6 / 63 (9.52%)	
occurrences (all)	1	6	
Ejaculation disorder (10014326)	Additional description: Ejaculation disorder (10014326)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Erection decreased (10015117)	Additional description: Erection decreased (10015117)		
subjects affected / exposed	1 / 64 (1.56%)	4 / 63 (6.35%)	
occurrences (all)	1	4	
Gynaecomastia (10018800)	Additional description: Gynaecomastia (10018800)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Haemospermia (10019025)	Additional description: Haemospermia (10019025)		
subjects affected / exposed	5 / 64 (7.81%)	0 / 63 (0.00%)	
occurrences (all)	5	0	
Painful ejaculation (10072353)	Additional description: Painful ejaculation (10072353)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Prostatitis (10036978)	Additional description: Prostatitis (10036978)		
subjects affected / exposed	5 / 64 (7.81%)	1 / 63 (1.59%)	
occurrences (all)	5	1	
Retrograde ejaculation (10038967)	Additional description: Retrograde ejaculation (10038967)		
subjects affected / exposed	0 / 64 (0.00%)	2 / 63 (3.17%)	
occurrences (all)	0	2	
Testicular pain (10043345)	Additional description: Testicular pain (10043345)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Psychiatric disorders			
Libido decreased (10024419)	Additional description: Libido decreased (10024419)		
subjects affected / exposed	2 / 64 (3.13%)	3 / 63 (4.76%)	
occurrences (all)	2	3	
Insomnia (10022437)	Additional description: Insomnia (10022437)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Investigations			
Elevated prostate specific antigen [PSA] (10014484)	Additional description: Elevated prostate specific antigen [PSA] (10014484)		

subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Prostate specific antigen increased (10036931)	Additional description: Prostate specific antigen increased (10036931)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Semen volume decreased (10039944)	Additional description: Semen volume decreased (10039944)		
subjects affected / exposed	0 / 64 (0.00%)	3 / 63 (4.76%)	
occurrences (all)	0	3	
Congenital, familial and genetic disorders			
Hydrocele (10020488)	Additional description: Hydrocele (10020488)		
subjects affected / exposed	2 / 64 (3.13%)	0 / 63 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Arrhythmia (10003119)	Additional description: Arrhythmia (10003119)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Bradycardia (10006093)	Additional description: Bradycardia (10006093)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Palpitation (10033556)	Additional description: Palpitation (10033556)		
subjects affected / exposed	0 / 64 (0.00%)	2 / 63 (3.17%)	
occurrences (all)	0	3	
Nervous system disorders			
Dizziness (10013573)	Additional description: Dizziness (10013573)		
subjects affected / exposed	1 / 64 (1.56%)	1 / 63 (1.59%)	
occurrences (all)	1	1	
Headache (10019211)	Additional description: Headache (10019211)		
subjects affected / exposed	1 / 64 (1.56%)	3 / 63 (4.76%)	
occurrences (all)	1	3	
Parasthesia (10033922)	Additional description: Parasthesia (10033922)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Syncope vasovagal (10042777)	Additional description: Syncope vasovagal (10042777)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	

Eye disorders			
Eye allergy (10015907)	Additional description: Eye allergy (10015907)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Digestion impaired (10012980)	Additional description: Digestion impaired (10012980)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Dryness oral (10013794)	Additional description: Dryness oral (10013794)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Haemorrhoids (10019022)	Additional description: Haemorrhoids (10019022)		
subjects affected / exposed	1 / 64 (1.56%)	1 / 63 (1.59%)	
occurrences (all)	2	1	
Nausea (10028813)	Additional description: Nausea (10028813)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Urticaria (10046735)	Additional description: Urticaria (10046735)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Bladder pain (10005063)	Additional description: Bladder pain (10005063)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Burning micturition (10006779)	Additional description: Burning micturition (10006779)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Dysuria (10013990)	Additional description: Dysuria (10013990)		
subjects affected / exposed	1 / 64 (1.56%)	1 / 63 (1.59%)	
occurrences (all)	1	1	
Haematuria (10018867)	Additional description: Haematuria (10018867)		
subjects affected / exposed	6 / 64 (9.38%)	0 / 63 (0.00%)	
occurrences (all)	7	0	
Renal colic (10038419)	Additional description: Renal colic (10038419)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	

Urinary tract disorder (10046566)	Additional description: Urinary tract disorder (10046566)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence (10046543)	Additional description: Urinary incontinence (10046543)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Urinary retention (10046555)	Additional description: Urinary retention (10046555)		
subjects affected / exposed	5 / 64 (7.81%)	0 / 63 (0.00%)	
occurrences (all)	5	0	
Musculoskeletal and connective tissue disorders			
Degenerative joint disease (10049491)	Additional description: Degenerative joint disease (10049491)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Rhinitis (10039083)	Additional description: Rhinitis (10039083)		
subjects affected / exposed	0 / 64 (0.00%)	2 / 63 (3.17%)	
occurrences (all)	0	2	
Sinusitis (10040753)	Additional description: Sinusitis (10040753)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Urinary infection (10046544)	Additional description: Urinary infection (10046544)		
subjects affected / exposed	5 / 64 (7.81%)	0 / 63 (0.00%)	
occurrences (all)	5	0	
Viral infection (10047461)	Additional description: Viral infection (10047461)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Gout (10018627)	Additional description: Gout (10018627)		
subjects affected / exposed	0 / 64 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
NIDDM (10029402)	Additional description: NIDDM (10029402)		
subjects affected / exposed	1 / 64 (1.56%)	0 / 63 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2011	Change in the treatment in case of allergy, modification of the flow-chart.
27 July 2011	Change of recrutment terms.
25 January 2012	Extension, changes related to vigilance.
19 December 2012	Extension.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29383480