Clinical trial results:
Study FDC114615: Comparative efficacy of DuodartTM plus lifestyle advice versus watchful waiting plus lifestyle advice with step-up therapy to tamsulosin in the management of treatment naïve men with moderately symptomatic benign prostatic hyperplasia and prostate enlargement.

Summary

EudraCT number	2010-022111-19
Trial protocol	DE ES NL GB FR GR IT
Global end of trial date	17 October 2013

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	03 December 2014

Trial information

Trial identification

Sponsor protocol code	FDC114615

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 866 435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 866 435-7343,

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	17 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of DUODART treatment plus lifestyle advice in providing superior symptomatic improvement to treatment naïve BPH subjects compared with watchful waiting plus lifestyle advice plus step-up therapy with tamsulosin.

Protection of trial subjects:

Over nine visits after Baseline vital signs, clinical labs (chemistry and hematology) and review of adverse events were collected to monitor participants' safety. Lifestyle advice to manage systems of benign prostatic hyperplasia (BPH) was also provided.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 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	Netherlands: 50
Country: Number of subjects enrolled	Romania: 79
Country: Number of subjects enrolled	Spain: 117
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	France: 99
Country: Number of subjects enrolled	Germany: 175
Country: Number of subjects enrolled	Greece: 89
Country: Number of subjects enrolled	Italy: 115
Worldwide total number of subjects	742
EEA total number of subjects	742

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	313
From 65 to 84 years	422
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Treatment-naïve men with symptomatic benign prostatic hyperplasia (BPH) meeting eligibility criteria were enrolled and were randomized in a 1:1 ratio to receive dutasteride plus tamsulosin once daily plus lifestyle advice or watchful waiting plus lifestyle advice.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dutasteride plus tamsulosin

Arm description:

Participants received a combination of dutasteride 0.5 milligrams (mg) plus tamsulosin 0.4 mg plus lifestyle advice for 24 months.

Arm type	Experimental
Investigational medicinal product name	Duodart
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.5 mg dutasteride + 0.4 mg tamsulosin, orally once daily after the same meal each day with a full glass of water.

Investigational medicinal product name	Tamsulosin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.4 mg orally, once daily after the same meal each day with a full glass of water.

Arm title	Watchful Waiting All: Escalated Yes and No

Arm description:

All participants were given lifestyle advice. If any International Prostate Symptom Score (IPSS) was the same or greater than the Baseline value at any study visit (post-randomization), participants received tamsulosin 0.4 mg once daily (Watchful Waiting Escalated=Yes). Tamsulosin was continued until the end of the study unless the participant elected to withdraw from the study. If participants did not receive tamsulosin, they were not classified as escalated (Watchful Waiting Escalated=No).

Arm type	Active comparator
Investigational medicinal product name	Tamsulosin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.4 mg orally, once daily after the same meal each day with a full glass of water.

Number of subjects in period 1	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No
Started	369	373
Completed	292	300
Not completed	77	73
Physician decision	6	11
Consent withdrawn by subject	28	28
Adverse event, non-fatal	28	13
Lost to follow-up	7	9
Lack of efficacy	7	5
Protocol deviation	1	7

Baseline characteristics

Reporting groups	
Reporting group title	Dutasteride plus tamsulosin
Reporting group description:	
Participants received a combination of dutasteride 0.5 milligrams (mg) plus tamsulosin 0.4 mg plus lifestyle advice for 24 months.	
Reporting group title	Watchful Waiting All: Escalated Yes and No
Reporting group description:	
All participants were given lifestyle advice. If any International Prostate Symptom Score (IPSS) was the same or greater than the Baseline value at any study visit (post-randomization), participants received tamsulosin 0.4 mg once daily (Watchful Waiting Escalated=Yes). Tamsulosin was continued until the end of the study unless the participant elected to withdraw from the study. If participants did not receive tamsulosin, they were not classified as escalated (Watchful Waiting Escalated=No).	

Reporting group values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No	Total
Number of subjects	369	373	742
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	66.3	66.2	
standard deviation	± 7.78	± 7.34	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	369	373	742
Race, Customized Units: Subjects			
White - White/Caucasian/European Heritage	357	363	720
White - Arabic/North African Heritage	4	2	6
African American/African Heritage	0	2	2
Mixed Race	0	1	1
Missing	8	5	13

End points

End points reporting groups

Reporting group title	Dutasteride plus tamsulosin

Reporting group description:

Participants received a combination of dutasteride 0.5 milligrams (mg) plus tamsulosin 0.4 mg plus lifestyle advice for 24 months.

Reporting group title	Watchful Waiting All: Escalated Yes and No

Reporting group description:

All participants were given lifestyle advice. If any International Prostate Symptom Score (IPSS) was the same or greater than the Baseline value at any study visit (post-randomization), participants received tamsulosin 0.4 mg once daily (Watchful Waiting Escalated=Yes). Tamsulosin was continued until the end of the study unless the participant elected to withdraw from the study. If participants did not receive tamsulosin, they were not classified as escalated (Watchful Waiting Escalated=No).

Subject analysis set title	Watchful Waiting Escalated=Yes
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All participants were given lifestyle advice. If any IPSS was the same or greater than the Baseline value at any study visit (post-randomization), participants received tamsulosin 0.4 mg once daily (Watchful Waiting Escalated=Yes). Tamsulosin was continued until the end of the study unless the participant elected to withdraw from the study.

Primary: Change from Baseline in the total International Prostate Symptom score (IPSS) at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the last observation carried forward (LOCF) approach

End point title	Change from Baseline in the total International Prostate Symptom score (IPSS) at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the last observation carried forward (LOCF) approach

End point description:

The IPSS questionnaire is a 7-item self-administered questionnaire designed to quantify the following urinary symptoms: Question 1 (Q1), incomplete emptying; Q2, frequency; Q3, intermittency; Q4, urgency; Q5, weak stream; Q6, straining; Q7, nocturia. It has an additional, independent eighth question to assess change in BPH-related health status (BHS) and quality of life. BHS scores range from 0 to 6, where 0 indicates "delighted" and 6 indicates "terrible." The 7 items in the IPSS questionnaire quantitatively measure the level of urinary symptoms reported as a total IPSS. The total IPSS (sum of the first 7 items) can range from 0 to 35: mild (0 to 7), moderate (8 to 19), or severe (20 to 35). Change from Baseline in IPSS total score was calculated as the Month 24 value minus the Baseline value. LOCF analysis involves bringing forward the last non-missing post-Baseline assessment for a participant with missing data and/or for a participant who discontinued from the study.

End point type	Primary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359[1]	368[2]		
Units: Scores on a scale				
least squares mean (standard error)				
Month 1, n=358, 367	-3.2 (± 0.21)	-0.9 (± 0.2)		
Month 3, n=359, 368	-4.5 (± 0.22)	-2.4 (± 0.22)		

Month 6, n=359, 368	-4.6 (± 0.23)	-3.2 (± 0.22)		
Month 9, n=359, 368	-5.1 (± 0.22)	-3.6 (± 0.22)		
Month 12, n=359, 368	-5.2 (± 0.23)	-3.6 (± 0.23)		
Month 15, n=359, 368	-5.2 (± 0.25)	-3.6 (± 0.24)		
Month 18, n=359, 368	-5.1 (± 0.25)	-3.3 (± 0.25)		
Month 21, n=359, 368	-5.5 (± 0.25)	-3.6 (± 0.24)		
Month 24, n=359, 368	-5.4 (± 0.25)	-3.6 (± 0.25)		

Notes:

[1] - Intent-to-Treat (ITT) Population

[2] - Intent-to-Treat (ITT) Population

Statistical analyses

Statistical analysis title	Month 1
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001 [4]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-1.7
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[3] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.

[4] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 3
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.001 [6]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	-1.5
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[5] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.

[6] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 6
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.001 [8]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[7] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.

[8] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 9
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.001 [10]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.31

Notes:

[9] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.

[10] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 12
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No

Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	< 0.001 [12]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[11] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.

[12] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 15
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	< 0.001 [14]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[13] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.

[14] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 18
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	< 0.001 [16]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.35

Notes:

[15] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.
[16] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 21
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	< 0.001 [18]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[17] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.
[18] - Values are based on t-tests from the general linear model.

Statistical analysis title	Month 24
Comparison groups	Dutasteride plus tamsulosin v Watchful Waiting All: Escalated Yes and No
Number of subjects included in analysis	727
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.001 [20]
Method	t-test, 2-sided
Parameter estimate	Adjusted Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[19] - Estimates are based on the adjusted means from the general linear model: Change from Baseline = Treatment + Cluster + Baseline Value. The adjusted mean difference is based on dutasteride plus tamsulosin minus Watchful Waiting All.

[20] - Values are based on t-tests from the general linear model.

Secondary: Number of participants with change from Baseline in the indicated improvement categories in the IPSS at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point title	Number of participants with change from Baseline in the indicated improvement categories in the IPSS at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point description:

Symptom improvement was assessed using IPSS categorical changes from Baseline. Change from Baseline categories were summarized by treatment group using five improvement levels: >=1 point through >=5 points. IPSS percent change from Baseline was summarized using seven improvement levels: >0 percent, >=10 percent, >=20 percent, >=25 percent, >=30 percent, >=40 percent, and >=50 percent. Change in IPSS from Baseline was analysed using the LOCF method and is summarized for the following categories: >=2 points, >=3 points, and percent change >=25. The 7 items in the IPSS questionnaire quantitatively measure the level of urinary symptoms reported as a total IPSS. The total IPSS (sum of the first 7 items) can range from 0 to 35: mild (0 to 7), moderate (8 to 19), or severe (20 to 35).

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359[21]	368[22]		
Units: participants				
Month 1, >=2 points, n=358, 367	225	149		
Month 1, >=3 points, n=358, 367	182	90		
Month 1, >=25 percent, n=358, 367	161	76		
Month 3, >=2 points, n=359, 368	277	221		
Month 3, >=3 points, n=359, 368	233	172		
Month 3, >=25 percent, n= 359, 368	218	150		
Month 6, >=2 points, n=359, 368	277	250		
Month 6, >=3 points, n=359, 368	245	208		
Month 6, >=25 percent, n=359, 368	229	189		
Month 9, >=2 points, n=359, 368	286	276		
Month 9, >=3 points, n=359, 368	257	222		
Month 9, >=25 percent, n=359, 368	247	207		
Month 12, >=2 points, n=359, 368	291	273		
Month 12, >=3 points, n=359, 368	261	229		
Month 12, >=25 percent, n= 359, 368	249	214		
Month 15, >=2 points, n=359, 368	289	275		
Month 15, >=3 points, n=359, 368	259	243		
Month 15, >=25 percent, n=359, 368	245	231		
Month 18, >=2 points, n=359, 368	288	268		
Month 18, >=3 points, n=359, 368	262	229		
Month 18, >=25 percent, n=359, 368	245	212		

Month 21, >=2 points, n=359, 368	292	274		
Month 21, >=3 points, n=359, 368	267	237		
Month 21, >=25 percent, n= 359, 368	253	224		
Month 24, >=2 points, n=359, 368	295	279		
Month 24, >=3points, n=359, 368	277	234		
Month 24, >=25 percent, n= 359, 368	261	221		

Notes:

[21] - ITT Population

[22] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the BPH Impact Index (BII) score at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point title	Change from Baseline in the BPH Impact Index (BII) score at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point description:

The BII is a 4-item questionnaire covering physical discomfort, worry, bother, and impact on usual activities, with a minimum score of 0 (best) and a maximum score (worst) of 13 points. Individual missing questionnaire responses were imputed, as applicable. Change from Baseline in the BII score was summarized by treatment group using the LOCF approach at each scheduled post-Baseline assessment. LOCF analysis involves bringing forward the last non-missing post-Baseline assessment for a participant with missing data and/or for a participant who discontinued from the study. Estimates are based on the adjusted means from the general linear model: Change from Baseline =Treatment + Cluster + Baseline Value. Baseline is defined as the Visit 2 value if it exists; otherwise, it is the latest of all Screening values. Change from Baseline was calculated as the post-Baseline vaue minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359[23]	368[24]		
Units: Scores on a scale				
least squares mean (standard error)				
Month 1, n=357, 366	-1.3 (± 0.11)	-0.4 (± 0.11)		
Month 3, n=359, 368	-1.8 (± 0.11)	-1 (± 0.11)		
Month 6, n=359, 368	-1.9 (± 0.11)	-1.3 (± 0.11)		
Month 9, n=359, 368	-2.1 (± 0.11)	-1.5 (± 0.11)		
Month 12, n=359, 368	-2.1 (± 0.12)	-1.5 (± 0.12)		
Month 15, n=359, 368	-2.2 (± 0.12)	-1.5 (± 0.12)		
Month 18, n=359, 368	-2.2 (± 0.12)	-1.4 (± 0.12)		
Month 21, n=359, 368	-2.4 (± 0.12)	-1.6 (± 0.12)		
Month 24, n=359, 368	-2.4 (± 0.12)	-1.6 (± 0.12)		

Notes:

[23] - ITT Population

[24] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the BPH-related Health Status (BHS) score at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point title	Change from Baseline in the BPH-related Health Status (BHS) score at Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point description:

Each participant was asked the following question "If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?". This response was rated from 0 ("delighted") to 6 ("terrible"). Change from Baseline in the BHS score was summarized by treatment group using the LOCF approach at each scheduled post-Baseline assessment. LOCF analysis involves bringing forward the last non-missing post-Baseline assessment for a participant with missing data and/or for a participant who discontinued from the study. Estimates are based on the adjusted means from the general linear model: Change from Baseline =Treatment + Cluster + Baseline Value. Baseline is defined as the Visit 2 value if it exists; otherwise, it is the latest of all Screening values. Change from Baseline was calculated as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359[25]	368[26]		
Units: Scores on a scale				
least squares mean (standard error)				
Month 1, n=358, 367	-0.8 (± 0.06)	-0.3 (± 0.05)		
Month 3, n=359, 368	-1.1 (± 0.06)	-0.7 (± 0.06)		
Month 6, n=359, 368	-1.2 (± 0.06)	-0.9 (± 0.06)		
Month 9, n=359, 368	-1.3 (± 0.06)	-1 (± 0.06)		
Month 12, n=359, 368	-1.3 (± 0.06)	-1.1 (± 0.06)		
Month 15, n=359, 368	-1.4 (± 0.06)	-1.1 (± 0.06)		
Month 18, n=359, 368	-1.4 (± 0.06)	-1.1 (± 0.06)		
Month 21, n=359, 368	-1.5 (± 0.06)	-1.1 (± 0.06)		
Month 24, n=359, 368	-1.5 (± 0.06)	-1.1 (± 0.06)		

Notes:

[25] - ITT Population

[26] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of events of clinical progression (CP) of BPH

End point title	Number of events of clinical progression (CP) of BPH

End point description:

The number of participants with the first occurrence of clinical progression (CP) of BPH occurring on or after the randomization date are summarized by treatment and year. Time is based on the date of the first-occurring CP event, and is relative to the randomization date. CP of BPH is a composite of five endpoints assessed through the end of the study, including: symptom deterioration by IPSS >=3 points from Baseline (Visit 2); acute urinary retention related to BPH; incontinence (overflow or urge) related to BPH; recurrent urinary tract infection (UTI) or urosepsis related to BPH; renal insufficiency related to BPH (a single >=50% rise from Baseline serum creatinine and a total value >=1.5 milligrams/deciliter). For components that required multiple episodes, the first of the multiple episodes was utilized in terms of timing.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[27]	373[28]		
Units: events				
Year 1, n=369, 373	48	94		
Year 2, n=276, 251	17	14		

Notes:

[27] - ITT Population. Only those participants at risk for CP at the specified visit were analyzed.

[28] - ITT Population. Only those participants at risk for CP at the specified visit were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who had any BPH-related surgery, who had the indicated type of surgery, who had 2 BPH-related surgeries, and who had >=3 BPH-related surgeries

End point title	Number of participants who had any BPH-related surgery, who had the indicated type of surgery, who had 2 BPH-related surgeries, and who had >=3 BPH-related surgeries

End point description:

BPH-related surgery was summarized for events occurring on or after the date of randomization. The number of participants who had any BPH-related surgery, the indicated type of surgery, and multiple surgeries was summarized by treatment. Type of surgery data (cystoscopy, transurethral resection of the prostate [TURP], and prostatectomy) are presented in terms of the first-occurring BPH-related surgery after randomization. It was possible for a single participant to have multiple surgeries.

End point type	Secondary

End point timeframe:

Up to Month 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[29]	373[30]		
Units: participants				
Participants with any BPH-related surgery	6	3		
Participants with cystoscopy	5	1		
Participants with TURP	2	1		
Participants with prostatectomy	0	1		
Participants with 2 surgeries	1	0		
Participants with >=3 surgeries	0	0		

Notes:

[29] - ITT Population

[30] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated responses to Question 1 of the Patient Perception of Study Treatment (PPST) questionnaire at Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point title	Number of participants with the indicated responses to Question 1 of the Patient Perception of Study Treatment (PPST) questionnaire at Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point description:

The PPST questionnaire consists of two questions (asked to determine how satisfied participants are with the treatment received) and was administered at Baseline and all post-Baseline visits. Question 1 was: "Overall, how satisfied are you with the treatment and its effect on your urinary problems?" There were seven possible responses, including: "very satisfied," "satisfied," "somewhat satisfied," neutral," "somewhat dissatisfied," "dissatisfied," and "very dissatisfied." Response categories were created by grouping together "very satisfied," "satisfied," and "somewhat satisfied" responses into the category of "Any Satisfaction (AS)," and separately grouping "neutral," "somewhat dissatisfied," "dissatisfied," and "very dissatisfied" responses into the category of "Neutral or Any Dissatisfaction (N/AD)." The LOCF method involves bringing forward the last non-missing post-Baseline assessment for a participant with missing data and/or for a participant who discontinued from the study.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359[31]	364[32]		
Units: participants				
Baseline, Any Satisfaction, n=315, 328	119	122		
Baseline, Neutral/Any Dissatisfaction, n=315, 328	196	206		
Month 1, Any Satisfaction, n=358, 349	272	209		

Month 1, Neutral/Any Dissatisfaction, n=358, 349	86	140		
Month 3, Any Satisfaction, n= 359, 359	300	265		
Month 3, Neutral/Any Dissatisfaction, n=359, 359	59	94		
Month 6, Any Satisfaction, n=359, 361	301	285		
Month 6, Neutral /Any Dissatisfaction, n=359, 361	58	76		
Month 9, Any Satisfaction, n=359, 361	304	293		
Month 9, Neutral/Any Dissatisfaction, n= 359, 361	55	68		
Month 12, Any Satisfaction, n=359, 363	311	305		
Month 12, Neutral/Any Dissatisfaction, n=359, 363	48	58		
Month 15, Any Satisfaction, n=359, 364	311	299		
Month 15, Neutral/Any Dissatisfaction, n=359, 364	48	65		
Month 18, Any Satisfaction, n=359, 364	305	298		
Month 18, Neutral/Any Dissatisfaction, n=359, 364	54	66		
Month 21, Any Satisfaction, n=359, 364	310	300		
Month 21, Neutral/Any Dissatisfaction, n=359, 364	49	64		
Month 24, Any Satisfaction, n=359, 364	312	312		
Month 24, Neutral/Any Dissatisfaction, n=359, 364	47	52		

Notes:

[31] - ITT Population

[32] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated responses to Question 2 of the Patient Perception of Study Treatment (PPST) questionnaire at Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point title	Number of participants with the indicated responses to Question 2 of the Patient Perception of Study Treatment (PPST) questionnaire at Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24 using the LOCF approach

End point description:

The PPST questionnaire consists of two questions (asked to determine how satisfied participants are with the treatment received) and was administered at Baseline and all post-Baseline visits. Question 2 was: "Would you ask your doctor for the treatment you received in this study?" There were three possible responses, including: "Yes," "No," and "Not sure." Response categories included "Yes" and "No or Not Sure," created by grouping together "No" and "Not sure." The LOCF method involves bringing forward the last non-missing post-Baseline assessment for a participant with missing data and/or for a participant who discontinued from the study.

End point type	Secondary

End point timeframe:

Baseline and Months 1, 3, 6, 9, 12, 15, 18, 21, and 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359[33]	364[34]		
Units: participants				
Baseline, Yes, n=315, 328	109	103		
Baseline, No or Not Sure, n=315, 328	206	225		
Month 1, Yes, n=358, 347	224	166		
Month 1, No or Not Sure, n=358, 347	134	181		
Month 3, Yes, n=359, 357	232	207		
Month 3, No or Not Sure, n=359, 357	127	150		
Month 6, Yes, n=359, 360	232	227		
Month 6, No or Not Sure, n=359, 360	127	133		
Month 9, Yes, n=359, 361	238	231		
Month 9, No or Not Sure, n=359, 361	121	130		
Month 12, Yes, n=359, 363	240	229		
Month 12, No or Not Sure, n=359, 363	119	134		
Month 15, Yes, n=359, 364	246	239		
Month 15, No or Not Sure, n=359, 364	113	125		
Month 18, Yes, n=359, 364	235	236		
Month 18, No or Not Sure, n=359, 364	124	128		
Month 21, Yes, n=359, 364	249	234		
Month 21, No or Not Sure, n=359, 364	110	130		
Month 24, Yes, n=359, 364	243	236		
Month 24, No or Not Sure, n=359, 364	116	128		

Notes:

[33] - ITT Population

[34] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Exposure to study drug

End point title	Exposure to study drug

End point description:

Study drug exposure (days) = treatment stop date - treatment start date + 1. Participants in the Watchful Waiting Escalated=Yes subgroup could have been escalated to study drug at any time during the study. Therefore, it is possible that participants were exposed to tamsulosin for a shorter length of time than participants in the dutasteride plus tamsulosin group.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	368[35]	229[36]		
Units: days				
arithmetic mean (standard deviation)	639.8 (± 215.49)	566.3 (± 195.13)		

Notes:

[35] - Treated Subjects Population

[36] - Treated Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated first-occurring component of clinical progression (CP) of BPH

End point title	Number of participants with the indicated first-occurring component of clinical progression (CP) of BPH

End point description:

CP of BPH is a composite of five endpoints assessed through the end of the study, including: symptom progression (symptom deterioration by IPSS >=3 points from Baseline [Visit 2]); acute urinary retention (AUR) related to BPH; incontinence (overflow or urge) related to BPH; recurrent urinary tract infection (UTI) or urosepsis related to BPH; renal insufficiency related to BPH (a single >=50% rise from Baseline serum creatinine and a total value >=1.5 milligrams/deciliter). The number of participants with CP of BPH, the number of participants with the indicated first-occurring component of CP of BPH, the number of participants with two simultaneously first-occurring components ("Tied for first component"), and the number of participants with multiple first-occurring components were summarized by treatment group.

End point type	Secondary

End point timeframe:

Up to Month 24

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[37]	373[38]		
Units: participants				
Participants with CP of BPH, n=369, 373	65	108		
BPH symptom progression, n=65, 108	59	97		
BPH-related AUR, n=65, 108	2	4		
BPH-related incontinence, n=65, 108	4	3		
Recurrent BPH-related UTI, n=65, 108	0	4		
BPH-related renal insufficiency, n=65, 108	0	0		
Tied for first component, n=65, 108	0	0		
2 components, n=65, 108	4	9		
3 components, n=65, 108	0	1		
>=4 components, n=65, 108	0	1		

Notes:

[37] - ITT Population

[38] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE) starting post-randomization

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE) starting post-randomization

End point description:

A post-randomization adverse event is defined as an event with an onset on or after the randomization date or with a missing onset date. An AE is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or is a congenital anomaly/birth defect. Medical or scientific judgment was exercised in deciding whether reporting was appropriate in other situations. Refer to the general non-serious AE/SAE module for a list of non-serious AEs (occurring at a frequency threshold of >=5%) and SAEs.

End point type	Secondary

End point timeframe:

Up to 2 years

End point values	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No	Watchful Waiting Escalated=Yes	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	369[39]	373[40]	229[41]	
Units: participants				
Any AE	190	119	95	
Any SAE	38	25	19	

Notes:

[39] - ITT Population

[40] - ITT Population

[41] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious adverse events (AEs) starting post-randomization (including events with an onset on or after the randomization date or with a missing onset date) were collected (up to 2 years).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Dutasteride plus tamsulosin

Reporting group description:

Participants received a combination of dutasteride 0.5 milligrams (mg) plus tamsulosin 0.4 mg plus lifestyle advice for 24 months.

Reporting group title	Watchful Waiting All: Escalated Yes and No

Reporting group description:

All participants were given lifestyle advice. If any International Prostate Symptom Score (IPSS) was the same or greater than the Baseline value at any study visit (post-randomization), participants received tamsulosin 0.4 mg once daily (Watchful Waiting Escalated=Yes). Tamsulosin was continued until the end of the study unless the participant elected to withdraw from the study.

Reporting group title	Watchful Waiting Escalated=Yes

Reporting group description:

All participants were given lifestyle advice. If any IPSS was the same or greater than the Baseline value at any study visit (post-randomization), participants received tamsulosin 0.4 mg once daily (Watchful Waiting Escalated=Yes). Tamsulosin was continued until the end of the study unless the participant elected to withdraw from the study.

Serious adverse events	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No	Watchful Waiting Escalated=Yes
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 369 (10.30%)	25 / 373 (6.70%)	19 / 229 (8.30%)
number of deaths (all causes)	0	3	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 369 (0.00%)	2 / 373 (0.54%)	2 / 229 (0.87%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 369 (0.00%)	2 / 373 (0.54%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

B-cell lymphoma			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Bronchial carcinoma			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Metastases to liver			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Hepatocellular carcinoma			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Myxoid liposarcoma			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
General disorders and administration			

site conditions			
Chest pain			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Death			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pyrexia			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 369 (0.27%)	2 / 373 (0.54%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 369 (0.27%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Respiratory acidosis			

subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Contusion			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Post procedural haemorrhage			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Wound			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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

Lower limb fracture			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Post procedural haematuria			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Craniocerebral injury			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	4 / 369 (1.08%)	2 / 373 (0.54%)	2 / 229 (0.87%)
occurrences causally related to treatment / all	1 / 4	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 369 (0.27%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Aortic valve stenosis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Atrioventricular block			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Cardiomyopathy			

subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Coronary artery disease			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Tachyarrhythmia			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart valve incompetence			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	0 / 229 (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
Nervous system disorders			
Presyncope			
subjects affected / exposed	2 / 369 (0.54%)	0 / 373 (0.00%)	0 / 229 (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
Syncope			
subjects affected / exposed	1 / 369 (0.27%)	1 / 373 (0.27%)	0 / 229 (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
Transient ischaemic attack			

subjects affected / exposed	1 / 369 (0.27%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar infarction			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Sciatica			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia megaloblastic			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Lymphadenopathy			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Ulcerative keratitis			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	2 / 369 (0.54%)	1 / 373 (0.27%)	0 / 229 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Anal fistula			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Gastritis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Ileus			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Pancreatitis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Pancreatitis acute			

subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis necrotising			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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 and urinary disorders			
Calculus bladder			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoarthritis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Polymyalgia rheumatica			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 369 (0.27%)	2 / 373 (0.54%)	2 / 229 (0.87%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 369 (0.54%)	0 / 373 (0.00%)	0 / 229 (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
Diverticulitis			
subjects affected / exposed	0 / 369 (0.00%)	2 / 373 (0.54%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Pilonidal cyst			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Pneumonia			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 369 (0.27%)	0 / 373 (0.00%)	0 / 229 (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
Infected cyst			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal sepsis			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	0 / 369 (0.00%)	1 / 373 (0.27%)	1 / 229 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Dutasteride plus tamsulosin	Watchful Waiting All: Escalated Yes and No	Watchful Waiting Escalated=Yes
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 369 (11.65%)	13 / 373 (3.49%)	12 / 229 (5.24%)
Reproductive system and breast disorders			
Retrograde ejaculation			
subjects affected / exposed	19 / 369 (5.15%)	10 / 373 (2.68%)	10 / 229 (4.37%)
occurrences (all)	19	10	10
Erectile dysfunction			
subjects affected / exposed	31 / 369 (8.40%)	4 / 373 (1.07%)	3 / 229 (1.31%)
occurrences (all)	32	4	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 July 2011	This amendment applied to all sites and all countries and was implemented after 496 participants had been randomized into the study. The changes in this amendment included adding an additional PSA test at Visit 5 and including some additional notes regarding the timing of biopsy.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported