Clinical trial results:
Reporting and Analysis Plan for FDC116115: A prospective study of sexual function in sexually active men treated for BPH

Summary

EudraCT number	2012-002047-26
Trial protocol	GR NL HU ES DE
Global end of trial date	05 April 2016

Results information

Result version number	v1 (current)
This version publication date	01 December 2016
First version publication date	01 December 2016

Trial information

Trial identification

Sponsor protocol code	116115

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	31 May 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 April 2016
Global end of trial reached?	Yes
Global end of trial date	05 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the change in sexual function from baseline to 1 year in sexually active men with at least moderate BPH (international prostate symptom score - IPSS = or > 12) who are treated with DUODART, compared to men treated with placebo

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 February 2013
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	Australia: 32
Country: Number of subjects enrolled	France: 54
Country: Number of subjects enrolled	Germany: 72
Country: Number of subjects enrolled	Greece: 65
Country: Number of subjects enrolled	Hungary: 81
Country: Number of subjects enrolled	Netherlands: 74
Country: Number of subjects enrolled	Spain: 111
Worldwide total number of subjects	489
EEA total number of subjects	457

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)	210
From 65 to 84 years	278
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This is a European double-blind, placebo-controlled, parallel-group study to assess the impact of dutasteride treatment on sexual function in men with moderate/severe Benign Prostatic Hyperplasia (BPH)

Pre-assignment

Screening details:

Eligible participants (par.) entered a 4-week Placebo Run-in Phase, and were randomised in 1:1 ratio to receive DUODART (fixed dose combination of dutasteride 0.5 mg and tamsulosin 0.4 mg) and placebo one capsule daily for 52 weeks. Follow-up was performed 6 months after the last dose of study medication

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received a matching placebo for Duodart plus lifestyle advice for 12 months

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Sugar capsule was administered once daily

Arm title	Duodart

Arm description:

Participants received a combination of dutasteride 0.5 milligrams (mg) and tamsulosin 0.4 mg plus lifestyle advice for 12 months

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

Dosage and administration details:

DUODART (fixed dose combination of dutasteride 0.5mg and tamsulosin 0.4mg) was administered once daily

Number of subjects in period 1	Placebo	Duodart
Started	246	243
Completed	191	184
Not completed	55	59
Physician decision	5	2
Consent withdrawn by subject	9	9
Adverse event, non-fatal	24	33
Participants reached stopping criteria	1	1
Lost to follow-up	4	-
Lack of efficacy	8	10
Protocol deviation	4	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received a matching placebo for Duodart plus lifestyle advice for 12 months	
Reporting group title	Duodart
Reporting group description:	
Participants received a combination of dutasteride 0.5 milligrams (mg) and tamsulosin 0.4 mg plus lifestyle advice for 12 months	

Reporting group values	Placebo	Duodart	Total
Number of subjects	246	243	489
Age categorical			
Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	65.4	65.7	
standard deviation	± 6.49	± 6.59	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	0	0	0
Male	246	243	489
Race/Ethnicity, Customized			
Units: Subjects			
African American/African Heritage	1	2	3
American Indian or Alaska Native	2	3	5
Asian - East Asian Heritage	1	0	1
White - Arabic/North African Heritage	3	0	3
White - White/Caucasian/European Heritage	239	237	476
Mixed Race	0	1	1

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received a matching placebo for Duodart plus lifestyle advice for 12 months	
Reporting group title	Duodart
Reporting group description:	
Participants received a combination of dutasteride 0.5 milligrams (mg) and tamsulosin 0.4 mg plus lifestyle advice for 12 months	

Primary: Changes from Baseline (BL) in total score from the full Men's Sexual Health Questionnaire (MSHQ) at 12 months

End point title	Changes from Baseline (BL) in total score from the full Men's Sexual Health Questionnaire (MSHQ) at 12 months
End point description:	
Total MSHQ score is composed of 3 domain scores: Erection score(ES)=sum of score for Questions (Q) 1 to 3(ranges from 0 to 15), Ejaculation score(EjS)=sum of scores for Q5 to 11(ranges from 1 to 35), Satisfaction score(SS)=sum of scores for Q13 to 18(ranges from 6 to 30). Total MSHQ score=ES+EjS+SS. The total MSHQ score ranges from 7-80, with higher scores indicating greater sexual function. Change from BL at scheduled post-BL time points were analyzed using a mixed model repeated measures (MMRM) analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest double-blind (DB) treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Month 12 value(s) minus BL value(s)	
End point type	Primary
End point timeframe:	
Baseline and 12 months	

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162[1]	151		
Units: Scores on a scale				
least squares mean (standard error)	-0.7 (± 0.78)	-8.7 (± 0.81)		

Notes:

[1] - Intent-to-Treat (ITT): All randomized par. regardless of whether or not treatment was administered

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Placebo v Duodart

Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.22
upper limit	-5.79

Secondary: Change from baseline in scores from the full Men's Sexual Health Questionnaire (MSHQ) at 1, 3, 6 and 9 months

End point title	Change from baseline in scores from the full Men's Sexual Health Questionnaire (MSHQ) at 1, 3, 6 and 9 months

End point description:

Total MSHQ score is composed of 3 domain scores: ES=sum of score for Q 1 to 3(ranges from 0 to 15), EjS=sum of scores for Q5 to 11(ranges from 1 to 35), SS=sum of scores for Q13 to 18(ranges from 6 to 30). Total MSHQ score=ES+EjS+SS and the score ranges from 7-80, with higher scores indicating greater sexual function. Change from BL at scheduled post-BL time points were analysed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Month 1, 3, 6, 9 values minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and up to 9 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[2]	243		
Units: Scores on a scale				
least squares mean (standard error)				
Month 1, n=193, 192	-0.5 (± 0.68)	-4.6 (± 0.69)		
Month 3, n= 184, 181	-0.5 (± 0.72)	-6.9 (± 0.73)		
Month 6, n=179, 164	-0.8 (± 0.8)	-9.9 (± 0.83)		
Month 9, n=166, 146	-0.8 (± 0.76)	-9.6 (± 0.79)		

Notes:

[2] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description: Month 1	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-4.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.01
upper limit	-2.21

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Month 3	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Adjusted mean difference
Parameter estimate	Adjusted mean difference
Point estimate	-6.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.45
upper limit	-4.41

Statistical analysis title	Statistical analysis 3
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-9.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.31
upper limit	-6.77

Notes:

[3] - Month 6

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Month 9

Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-8.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.96
upper limit	-6.67

Secondary: Number of participants reaching various thresholds of change in total MSHQ from baseline at 12 months

End point title	Number of participants reaching various thresholds of change in total MSHQ from baseline at 12 months

End point description:

Participants reaching thresholds of change in total MSHQ were assessed. Threshold values are defined as multiplicative factor. Threshold included +10 points, +20 points, +25 points, -10 points, -20 points, -25 points; where "+" indicates improvement and "-"indicates worsening. Treatment comparisons were done based on categories defined by these thresholds using Mantel-Haenszel test

End point type	Secondary

End point timeframe:

Baseline and 12 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162[4]	151		
Units: Participants				
>= 25	0	1		
>= 20	3	3		
>= 10	16	8		
<= -25	3	13		
<= -20	3	20		

<= -10	24	61		

Notes:

[4] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in erectile dysfunction (ED) at 1, 3, 6, 9 and 12 months

End point title	Change from Baseline in erectile dysfunction (ED) at 1, 3, 6, 9 and 12 months

End point description:

Erection scale is a domain of MSHQ to assess erectile dysfunction. ES is the sum of score for questions 1 to 3. The score ranges from 0 (no erection) to 15 (strong erection). Change from BL at the scheduled post-baseline time points were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Month 1, 3, 6, 9 and 12 values minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[5]	243		
Units: Scores on a scale				
least squares mean (standard error)				
Month 1, n=209, 215	-0.3 (± 0.15)	-0.5 (± 0.15)		
Month 3, n= 202, 208	-0.5 (± 0.17)	-0.7 (± 0.17)		
Month 6, n= 193, 188	-0.6 (± 0.18)	-1 (± 0.19)		
Month 9, n=182, 169	-0.5 (± 0.18)	-1.2 (± 0.19)		
Month 12, n= 175, 168	-0.5 (± 0.19)	-1 (± 0.19)		

Notes:

[5] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Month 1

Comparison groups	Placebo v Duodart

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.23

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Month 3	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	0.24

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Month 6	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.88
upper limit	0.15

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Month 9	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.19
upper limit	-0.17

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Month 12	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.091
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.99
upper limit	0.07

Secondary: Change from Baseline in ejaculatory dysfunction (EjD) at 1, 3, 6, 9 and 12 months

End point title	Change from Baseline in ejaculatory dysfunction (EjD) at 1, 3, 6, 9 and 12 months

End point description:

Ejaculation scale is a domain of MSHQ to assess ejaculatory dysfunction. EjS is the sum of score for questions 5 to 11. The score ranges from 1 (could not ejaculate) to 35 (strong ejaculation). Change from BL at the scheduled post-baseline time points were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as

earliest DB treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Month 1, 3, 6, 9 and 12 values minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[6]	243		
Units: Scores on a scale				
least squares mean (standard error)				
Month 1, n=210, 208	-0.3 (± 0.42)	-3.2 (± 0.43)		
Month 3, n= 197, 196	-0.5 (± 0.48)	-5.8 (± 0.48)		
Month 6, n= 191, 179	-0.7 (± 0.53)	-7.5 (± 0.54)		
Month 9, n=177, 161	-0.5 (± 0.52)	-7.6 (± 0.53)		
Month 12, n= 173, 164	-0.6 (± 0.55)	-7.5 (± 0.56)		

Notes:

[6] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Month 1

Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-2.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.07
upper limit	-1.7

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Month 3

Comparison groups	Duodart v Placebo

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-5.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.59
upper limit	-3.9

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Month 6	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-6.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.3
upper limit	-5.34

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Month 9	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-7.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.51
upper limit	-5.59

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Month 12	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-6.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.47
upper limit	-5.38

Secondary: Change from Baseline in satisfaction score at 1, 3, 6, 9 and 12 months

End point title	Change from Baseline in satisfaction score at 1, 3, 6, 9 and 12 months

End point description:

Satisfaction scale is a domain of MSHQ to assess sexual relationship. SS is the sum of score for questions 13 to 18. The score ranges from 6 (extremely dissatisfied) to 30 (extremely satisfied). Change from BL at the scheduled post-baseline time points were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Month 1, 3, 6, 9 and 12 values minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[7]	243		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Month 1, n=200, 197	0.1 (± 0.26)	-0.8 (± 0.26)		
Month 3, n= 189, 182	0.4 (± 0.27)	-0.5 (± 0.28)		
Month 6, n= 185, 168	0.2 (± 0.3)	-1.5 (± 0.31)		
Month 9, n=173, 153	0 (± 0.3)	-1.2 (± 0.32)		
Month 12, n= 169, 152	0.3 (± 0.29)	-0.6 (± 0.3)		

Notes:
[7] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Month 1	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.67
upper limit	-0.21

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Month 3	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	-0.17

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Month 6	
Comparison groups	Placebo v Duodart

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.57
upper limit	-0.88

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Month 9	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	-0.3

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Month 12	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	-0.01

Secondary: Change from Baseline in International Prostate Symptom Score (IPSS) Scores using the Observed Cases approach at 2 weeks, 1, 3, 6, 9, and 12 months

End point title	Change from Baseline in International Prostate Symptom Score (IPSS) Scores using the Observed Cases approach at 2 weeks, 1, 3, 6, 9, and 12 months

End point description:

The IPSS questionnaire is a 7-item self-administered questionnaire designed to quantify urinary symptoms: Q1, incomplete emptying; Q2, frequency; Q3, intermittency; Q4, urgency; Q5, weak stream; Q6, straining; Q7, nocturia. The score can range from 0 to 35: mild (0 to 7), moderate (8 to 19), or severe (20 to 35). Change from BL were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Week 2, Months 1, 3, 6, 9 and 12 values minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[8]	243		
Units: Scores on a scale				
least squares mean (standard error)				
Week 2, n=232, 234	-1.5 (± 0.29)	-3.1 (± 0.29)		
Month1, n=222, 231	-2.8 (± 0.33)	-3.4 (± 0.33)		
Month 3, n=217, 224	-2.8 (± 0.33)	-4.1 (± 0.33)		
Month 6, n=206, 203	-2.9 (± 0.36)	-4.6 (± 0.36)		
Month 9, n=193, 185	-3.2 (± 0.38)	-4.5 (± 0.38)		
Month 12, n=187, 184	-3.2 (± 0.41)	-5.2 (± 0.41)		

Notes:

[8] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Week 2

Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.65

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.45
upper limit	-0.85

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Month 1	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.47
upper limit	0.37

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Month 3	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.19
upper limit	-0.36

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Month 6	
Comparison groups	Placebo v Duodart

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.74
upper limit	-0.72

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Month 9	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.28

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Month 12	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.12
upper limit	-0.83

Secondary: Change From Baseline in Quality of Life (BPH Impact Index –BII scores) at 2 weeks, 1, 3, 6, 9, and 12 months

End point title	Change From Baseline in Quality of Life (BPH Impact Index –BII scores) at 2 weeks, 1, 3, 6, 9, and 12 months

End point description:

The BPH Impact Index (BII) is a 4-item, self-administered questionnaire evaluating the impact of urinary problems on overall health and activity. Total scores range from 0 to 13; higher scores represent increased perceived impact of benign prostatic hyperplasia-lower urinary tract symptoms on overall health. Change from BL were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the subject took at least one dose of DB study drug; change from BL was calculated as Week 2, Months 1, 3, 6, 9 and 12 values minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[9]	243		
Units: Scores on a scale				
least squares mean (standard error)				
Week 2, n=226, 227	-0.3 (± 0.14)	-0.7 (± 0.14)		
Month1, n=216, 223	-0.7 (± 0.13)	-0.7 (± 0.13)		
Month 3, n=211, 217	-0.9 (± 0.15)	-1.1 (± 0.15)		
Month 6, n=201, 195	-0.6 (± 0.17)	-1.2 (± 0.17)		
Month 9, n=188, 179	-0.7 (± 0.16)	-1.2 (± 0.17)		
Month 12, n=183, 177	-0.6 (± 0.18)	-1.2 (± 0.18)		

Notes:

[9] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Week 2

Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.03

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Month 1	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.37

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Month 3	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	0.15

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Month 6	
Comparison groups	Duodart v Placebo

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	-0.15

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Month 9	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.056
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.91
upper limit	0.01

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Month 12	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	-0.08

Secondary: Change from Baseline in perception of treatment benefit/satisfaction with treatment (Patient Perception of Study Medication - PPSM questionnaire scores) at 2 weeks, 1, 3, 6, 9, and 12 months

End point title	Change from Baseline in perception of treatment benefit/satisfaction with treatment (Patient Perception of Study Medication - PPSM questionnaire scores) at 2 weeks, 1, 3, 6, 9, and 12 months

End point description:

Patient Perception of Study Medication (PPSM) is a 12-item questionnaire designed to quantify the participant's perceptions and satisfaction with the effect of study treatment on control of their urinary symptoms. The total PPSM score ranges from 7 to 49, with higher scores indicating lower satisfaction. Change from BL were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the subject took at least one dose of DB study drug; change from BL was calculated as Week 2, Months 1, 3, 6, 9, 12 values minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and up to 12 months

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[10]	243		
Units: Scores on a scale				
least squares mean (standard error)				
Week 2, n=225, 227	-0.4 (± 0.32)	-3.4 (± 0.32)		
Month1, n=216, 223	-1.3 (± 0.38)	-3.4 (± 0.38)		
Month 3, n=211, 217	-1.7 (± 0.41)	-3.8 (± 0.41)		
Month 6, n=201, 195	-1 (± 0.44)	-3.6 (± 0.44)		
Month 9, n=188, 179	-1.6 (± 0.45)	-2.9 (± 0.45)		
Month 12, n=182, 177	-1 (± 0.49)	-4.6 (± 0.49)		

Notes:

[10] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Week 2

Comparison groups	Duodart v Placebo

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.89
upper limit	-2.1

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Month 1	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.15
upper limit	-1.06

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Month 3	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-2.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.25
upper limit	-0.98

Statistical analysis title	Statistical analysis 4
Statistical analysis description: Month 6	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.76
upper limit	-1.3

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Month 9	
Comparison groups	Duodart v Placebo
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.56
upper limit	-0.05

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Month 12	
Comparison groups	Duodart v Placebo

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-3.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.87
upper limit	-2.14

Secondary: Change from baseline in total MSHQ scores from Baseline at 12 months among participants with IPSS improvement of >=2 points and >=3 points

End point title	Change from baseline in total MSHQ scores from Baseline at 12 months among participants with IPSS improvement of >=2 points and >=3 points

End point description:

Total MSHQ score is composed of 3 domain scores: ES+EjS+SS and the score ranges from 7-80, with higher scores indicating greater sexual function. Par. with change from baseline in total MSHQ scores with good BPH symptomatic response (measured by improvement in IPSS)were analysed. Change from BL at the scheduled post-baseline time points were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Month 12 value(s) minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[11]	243		
Units: Participants				
least squares mean (standard error)				
IPSS improvement of >=2, n=152, 142	-0.6 (± 0.81)	-8.4 (± 0.83)		
IPSS improvement of >=3, n=138,136	-0.6 (± 0.86)	-8 (± 0.86)		

Notes:

[11] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Par. with IPSS change from baseline >=2 points improvement at any time post-baseline visit

Comparison groups	Placebo v Duodart

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-7.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.07
upper limit	-5.49

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Par. with IPSS change from baseline >=3 points improvement at any time post-baseline visit	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-7.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.79
upper limit	-4.99

Secondary: Change from baseline in total MSHQ scores from Baseline at 12 months among participants with IPSS improvement of >=25 percent

End point title	Change from baseline in total MSHQ scores from Baseline at 12 months among participants with IPSS improvement of >=25 percent

End point description:

Participants with change from baseline in total MSHQ scores with good BPH symptomatic response (measured by improvement in IPSS)were analysed.Change from BL at the scheduled post-baseline time points were analyzed using MMRM analysis method with an Observed Cases approach. Values are expressed as adjusted mean along with standard error. The MMRM analysis included fixed categorical effects of treatment, visit and treatment by visit interaction and the continuous fixed covariates of BL total score and BL score by visit interaction. BL is defined as earliest DB treatment start date if the par. took at least one dose of DB study drug; change from BL was calculated as Month 12 value(s) minus BL value(s). Only those par with non-missing change from baseline data were analysed (presented as n=X,X in the category titles)

End point type	Secondary

End point timeframe:

Baseline and Month 12

End point values	Placebo	Duodart		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139[12]	133		
Units: Participants				
least squares mean (standard error)	-0.6 (± 0.86)	-8.3 (± 0.88)		

Notes:

[12] - ITT Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Par. with IPSS change from baseline >=25 points improvement at any time post-baseline visit	
Comparison groups	Placebo v Duodart
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	mixed-model repeated-measures
Parameter estimate	Adjusted mean difference
Point estimate	-7.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.22
upper limit	-5.35

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious Adverse Events (AEs) were collected from the start of study medication until follow-up (up to approximately 18 months).

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs are reported for ITT Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Duodart

Reporting group description:

Participants received a combination of dutasteride 0.5 mg and tamsulosin 0.4 mg plus lifestyle advice for 12 months

Reporting group title	Placebo

Reporting group description:

Participants received a matching placebo for Duodart plus lifestyle advice for 12 months

Serious adverse events	Duodart	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 243 (11.11%)	9 / 246 (3.66%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Prostatic adenoma			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal neoplasm			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Testicular cyst			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 243 (0.41%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 243 (0.41%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			

subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Presyncope			
subjects affected / exposed	2 / 243 (0.82%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fistula			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamic infarction			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			

subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertransaminasaemia			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	0 / 243 (0.00%)	1 / 246 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Spinal column stenosis			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 243 (0.82%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 243 (0.82%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected cyst			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory tract infection			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 243 (0.41%)	0 / 246 (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: 5 %

Non-serious adverse events	Duodart	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 243 (27.16%)	28 / 246 (11.38%)	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	24 / 243 (9.88%)	16 / 246 (6.50%)	
occurrences (all)	25	17	
Retrograde ejaculation			
subjects affected / exposed	23 / 243 (9.47%)	3 / 246 (1.22%)	
occurrences (all)	23	3	
Ejaculation disorder			
subjects affected / exposed	16 / 243 (6.58%)	2 / 246 (0.81%)	
occurrences (all)	16	2	
Psychiatric disorders			

Libido decreased subjects affected / exposed occurrences (all)	20 / 243 (8.23%) 22	12 / 246 (4.88%) 12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported