Clinical trial results:
PERMIXON® 160 mg hard capsule versus placebo in the treatment of symptomatic lower urinary tract symptoms due to benign prostatic hyperplasia.

Summary

EudraCT number	2014-000222-38
Trial protocol	IT ES CZ DE FR
Global end of trial date	27 June 2016
Results information	
Result version number	v1 (current)
This version publication date	12 July 2017
First version publication date	12 July 2017

Trial information

Trial identification	
Sponsor protocol code	P00048GP404
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	PIERRE FABRE MEDICAMENT
Sponsor organisation address	45 Place Abel Gance, Boulogne, France, 92100
Public contact	Montagne Agnes, Institut de Recherche Pierre Fabre, 33 534506350, agnes.montagne@pierre-fabre.com
Scientific contact	Montagne Agnes, Institut de Recherche Pierre Fabre, 33 534506350, agnes.montagne@pierre-fabre.com

Notes:

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2016
Global end of trial reached?	Yes
Global end of trial date	27 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare at 6 months (D180) the efficacy of PERMIXON® 160 mg b.i.d to a placebo in patients with lower urinary tract symptoms due to benign prostatic hyperplasia (LUTS/BPH) through the assessment of I-PSS.
This study was placebo-controlled and reference active treatment-controlled. The placebo group received the same medical care as the test active treatment group (Permixon) and the positive control group (Tamsulosin) according to that which would have been provided if they had not participated in the study.

Protection of trial subjects:

The study was performed in accordance with the current version of the Declaration of Helsinki (1964 and its subsequent amendments). The study was conducted in agreement with the International Conference on Harmonisation (ICH) guidelines on Good Clinical Practice (GCP), and with related national regulation in biomedical research.
The first study protocol in use (V1, 7 February 2014), and the patient information sheets were reviewed and approved by the appropriate IECs. There were no substantial subsequent amendments.
This study was placebo-controlled and active reference-controlled (see rationale in "Evidence for comparator caption". The placebo group received the same medical care as the test treatment group (Permixon) and the positive control group (Tamsulosin), according to that which would have been provided if they had not participated in the trial. Patients were free to withdraw from the study at any time for any reason. The investigator could decide to withdraw a patient from the study due to tolerability/safety/efficacy issues if it was felt to be in the patient’s best interests.

Background therapy:

In order to differentiate between treatment effects both on efficacy and safety during the comparative treatment phase, included patients were naïve to any prior treatment for LUTS/BPH.
There was no systematic concomitant administration of any other product than investigational products.

Evidence for comparator:

This study was placebo-controlled to demonstrate the efficacy of Permixon in treating LUTS/BPH. LUTS/BPH is not often a life-threatening condition. The primary treatment goal for BPH is to alleviate bothersome LUTS that result from prostatic enlargement and improve patients’ quality of life. alpha1-blockers, 5alpha reductase inhibitors (5 ARIs), antimuscarinics, and phosphodiesterase type 5 inhibitors, either alone or in combination, are the standards of care for uncomplicated bothersome LUTS/BPH unresponsive to behavioural management, but present safety/tolerability issues such as orthostatic hypotension and retrograde ejaculation for alpha1-blockers and sexual dysfunction for 5-ARIs. In this context, a placebo is the indicated comparator.
Tamsulosine Arrow LP 0.4 mg is the most widely used medication for the treatment of symptoms related to BPH and was found to be well tolerated and clinically effective on symptoms and urinary flow in several placebo-controlled trials at the dose of 0.4 mg/day; thus it was used as a positive control in order to validate the sensitivity of the study for all efficacy analyses.

Actual start date of recruitment	07 May 2014
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	Spain: 81
Country: Number of subjects enrolled	Czech Republic: 215
Country: Number of subjects enrolled	France: 190
Country: Number of subjects enrolled	Germany: 106
Country: Number of subjects enrolled	Italy: 192
Worldwide total number of subjects	784
EEA total number of subjects	784

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)	427
From 65 to 84 years	357
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

68 centres recruited patients: 18 in Italy, 18 in France, 12 in Germany, 12 in Spain, and 8 in the Czech Republic.. 811 patients were screened, 784 enrolled, 608 randomised. An additional 22 screened patients (12 enrolled, 2 randomised) from 1 centre in France (#0514) were excluded from all analyses due to serious breach of GCP and protocol.

Pre-assignment

Screening details:

Male patients aged 45-85 years with symptomatic LUTS/BPH (I-PSS score > 12 and QoL I-PSS ≥ 3); LUTS/BPH-treatment naïve; with no historical/concomitant urinary tract disease with a potential impact on the treatment response.
An I-PSS score change <3 during a 1-month placebo run-in period was required to enter the treatment period.

Period 1

Period 1 title	Placebo Run-in Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

As for the treatment period, blinding was ensured by a double dummy process i.e. identical:
- colour, size and aspect of placebo1 and Permixon capsules and of placebo2 and Tamsulosin capsules
- packaging, labelling and administration of study products.

Arms

Arm title	Placebo run-in

Arm description:

All patients enrolled

Arm type	Placebo
Investigational medicinal product name	Placebo 1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

BID administration: two capsules per day = one capsule in the morning and one capsule in the evening

Investigational medicinal product name	Placebo 2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QD administration: one capsule per day, in the morning

Number of subjects in period 1	Placebo run-in
Started	784
Completed	608
Not completed	176
Eligibility criteria not met	138
Consent withdrawn by subject	37
Other commitment (holiday, travel)	1

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Double-blinding was ensured by a double dummy process i.e. identical:
- colour, size and aspect of placebo1 and Permixon capsules and of placebo2 and Tamsulosin capsules
- packaging, labelling and administration of study products.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Patients randomised at Visit 2 to placebo

Arm type	Placebo
Investigational medicinal product name	Placebo 1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

BID administration: two capsules per day = one capsule in the morning and one capsule in the evening

Investigational medicinal product name	Placebo 2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

qd administration: one capsule per day in the morning

Arm title	Permixon

Arm description:

Patients randomised at Visit 2 to Permixon

Arm type	Experimental

Investigational medicinal product name	Permixon
Investigational medicinal product code	P0048
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

BID administration: two capsules per day = one capsule in the morning; one capsule in the evening

Arm title	Tamsulosin

Arm description:

Patients randomised at visit 2 to tamsulosin

Arm type	Positive control
Investigational medicinal product name	Tamsulosine Arrow LP 0.4 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

qd administration: 1 capsule per day in the morning

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Patients could enter the comparative treatment period only if they had completed Period 1 (run-in period) with an I-PSS change <3 during this period. Their Baseline efficacy characteristics were measured at the beginning of Period 2.

Number of subjects in period 2[2]	Placebo	Permixon	Tamsulosin
Started	202	201	205
Completed	177	170	173
Not completed	25	31	32
Eligibility criteria not met	2	5	4
Consent withdrawn by subject	6	9	4
Other commitment (holiday, travel)	2	1	1
Adverse event, non-fatal	5	6	14
Lack of efficacy	10	8	5
Protocol deviation	-	2	4

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Enrolled patients (n=784) were the patients entering the placebo run-in period Randomised patients (n=608) were the patients having completed the placebo run-in period with an I-PSS change <3 during this period. These patients could enter the comparative treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients randomised at Visit 2 to placebo	
Reporting group title	Permixon
Reporting group description:	
Patients randomised at Visit 2 to Permixon	
Reporting group title	Tamsulosin
Reporting group description:	
Patients randomised at visit 2 to tamsulosin	

Reporting group values	Placebo	Permixon	Tamsulosin
Number of subjects	202	201	205
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	62.6	63.4	62.8
standard deviation	± 8.6	± 8.5	± 8.5
Gender categorical Units: Subjects			
Female	0	0	0
Male	202	201	205
Time to BPH diagnosis Units: years			
arithmetic mean	1.66	1.94	1.86
standard deviation	± 3.28	± 3.58	± 3.52
I-PSS Units: Points			
arithmetic mean	17.5	17.3	17.6
standard deviation	± 3.6	± 3.6	± 4
QoL-I-PSS Units: Points			
arithmetic mean	3.8	3.8	3.9
standard deviation	± 1	± 0.8	± 0.9
MSF-4			

Units: Points			
arithmetic mean	8.2	8.1	7.6
standard deviation	± 4.6	± 4.7	± 4.7

Reporting group values	Total		
Number of subjects	608		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	0		
Male	608		
Time to BPH diagnosis			
Units: years			
arithmetic mean			
standard deviation	-		
I-PSS			
Units: Points			
arithmetic mean			
standard deviation	-		
QoL-I-PSS			
Units: Points			
arithmetic mean			
standard deviation	-		
MSF-4			
Units: Points			
arithmetic mean			
standard deviation	-		

Subject analysis sets	
Subject analysis set title	Randomised set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomised patients, whether treated or not, were analysed for efficacy

Reporting group values	Randomised set		
Number of subjects	608		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	62.9		
standard deviation	± 8.5		
Gender categorical Units: Subjects			
Female	0		
Male	608		
Time to BPH diagnosis Units: years			
arithmetic mean	1.82		
standard deviation	± 3.46		
I-PSS Units: Points			
arithmetic mean	17.5		
standard deviation	± 3.7		
QoL-I-PSS Units: Points			
arithmetic mean	3.9		
standard deviation	± 0.9		
MSF-4 Units: Points			
arithmetic mean	8		
standard deviation	± 4.6		

End points

End points reporting groups

Reporting group title	Placebo run-in
Reporting group description:	
All patients enrolled	
Reporting group title	Placebo
Reporting group description:	
Patients randomised at Visit 2 to placebo	
Reporting group title	Permixon
Reporting group description:	
Patients randomised at Visit 2 to Permixon	
Reporting group title	Tamsulosin
Reporting group description:	
Patients randomised at visit 2 to tamsulosin	
Subject analysis set title	Randomised set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomised patients, whether treated or not, were analysed for efficacy	

Primary: I-PSS change from baseline to D180 (permixon vs placebo)

End point title	I-PSS change from baseline to D180 (permixon vs placebo)[1]
End point description:	
I-PSS score (range: 0-35) measures LUTS. A decrease indicates an improvement of symptoms	
End point type	Primary
End point timeframe:	
From Baseline to Day 180	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Efficacy endpoints were analysed between Placebo and Permixon arms and between Placebo and Tamsulosin arms, separately; so they were also defined separately.

End point values	Placebo	Permixon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	201		
Units: Points				
least squares mean (standard error)	-4.41 (± 0.4)	-4.51 (± 0.4)		

Statistical analyses

Statistical analysis title	ANCOVA
Statistical analysis description:	
Covariance analysis after LOCF imputation of missing data. The model incorporated I-PSS score change during the run-in period and baseline I-PSS score as covariates and country as stratum factor.	
Comparison groups	Placebo v Permixon

Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.833
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	0.92
Variability estimate	Standard error of the mean
Dispersion value	0.52

Secondary: I-PSS change from baseline to D180 (tamsulosin vs placebo)

End point title	I-PSS change from baseline to D180 (tamsulosin vs placebo)[2]

End point description:

I-PSS score (range: 0-35) measures LUTS. A decrease indicates an improvement of symptoms

End point type	Secondary

End point timeframe:

From Baseline to Day 180

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were analysed between Placebo and Permixon arms and between Placebo and Tamsulosin arms, separately; so they were also defined separately.

End point values	Placebo	Tamsulosin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	205		
Units: Points				
least squares mean (standard error)	-4.48 (± 0.39)	-5.24 (± 0.38)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

Covariance analysis after LOCF imputation of missing data. The model incorporated I-PSS score change during the run-in period and baseline I-PSS score as covariates and country as stratum factor.

Comparison groups	Placebo v Tamsulosin

Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.133
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.75
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.5

Secondary: MSF-4 change from baseline to D180 (permixon vs placebo)

End point title	MSF-4 change from baseline to D180 (permixon vs placebo)[3]

End point description:

MSF4 total score (range: 0 to 5) measures male sexual function. An increase indicates a deterioration of the sexual function

End point type	Secondary

End point timeframe:

From Baseline to Day 180

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were analysed between Placebo and Permixon arms and between Placebo and Tamsulosin arms, separately; so they were also defined separately.

End point values	Placebo	Permixon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	201		
Units: Points				
least squares mean (standard error)	-0.28 (± 0.2)	0.06 (± 0.2)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

Analysis of covariance using LOCF imputation of missing data. The model incorporated baseline MSF-4 score as covariate and country as stratum factor.

Comparison groups	Permixon v Placebo

Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.187
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.84
Variability estimate	Standard error of the mean
Dispersion value	0.26

Secondary: MSF-4 change from baseline to D180 (tamsulosin vs placebo)

End point title	MSF-4 change from baseline to D180 (tamsulosin vs placebo)[4]

End point description:

MSF4 total score (range: 0 to 5) measures male sexual function. An increase indicates a deterioration of the sexual function

End point type	Secondary

End point timeframe:

From Baseline to Day 180

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were analysed between Placebo and Permixon arms and between Placebo and Tamsulosin arms, separately; so they were also defined separately.

End point values	Placebo	Tamsulosin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	205		
Units: Points				
least squares mean (standard error)	-0.26 (± 0.2)	0.59 (± 0.2)		

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

Analysis of covariance using LOCF imputation of missing data. The model incorporated the baseline MSF-4 score as covariate and country as stratum factor.

Comparison groups	Placebo v Tamsulosin

Number of subjects included in analysis	407
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.36
Variability estimate	Standard error of the mean
Dispersion value	0.27

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Over the treatment period (180 days +/- 10 days) for al AEs and + 30 days post-end of study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients randomised at Visit 2 to placebo and having taken at least one dose of study treatment	
Reporting group title	Permixon
Reporting group description:	
Patients randomised at Visit 2 to Permixon and having taken at least one dose of treatment	
Reporting group title	Tamsulosin
Reporting group description:	
Patients randomised at Visit 2 to Tamsulosin and having taken at least one dose of study treatment	

Serious adverse events	Placebo	Permixon	Tamsulosin
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 201 (2.99%)	4 / 199 (2.01%)	6 / 205 (2.93%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hypergammaglobulinaemia benign monoclonal			
subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (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
Lung neoplasm malignant			
subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 201 (0.00%)	1 / 199 (0.50%)	1 / 205 (0.49%)
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	0 / 201 (0.00%)	1 / 199 (0.50%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 201 (0.00%)	0 / 199 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (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			
Varicose vein			
subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (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	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (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 / 201 (0.00%)	0 / 199 (0.00%)	2 / 205 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 201 (0.00%)	0 / 199 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Prepuce dorsal slit			

subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (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
Varicose vein operation			
subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (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
Knee arthroplasty			
subjects affected / exposed	0 / 201 (0.00%)	1 / 199 (0.50%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Diverticulitis			
subjects affected / exposed	0 / 201 (0.00%)	1 / 199 (0.50%)	0 / 205 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device use error			
subjects affected / exposed	0 / 201 (0.00%)	0 / 199 (0.00%)	1 / 205 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	0 / 205 (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

Frequency threshold for reporting non-serious adverse events: 1.5 %

Non-serious adverse events	Placebo	Permixon	Tamsulosin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 201 (28.86%)	43 / 199 (21.61%)	52 / 205 (25.37%)
Vascular disorders			

Orthostatic hypotension			
subjects affected / exposed	9 / 201 (4.48%)	7 / 199 (3.52%)	3 / 205 (1.46%)
occurrences (all)	10	7	3
Hypertension			
subjects affected / exposed	1 / 201 (0.50%)	2 / 199 (1.01%)	3 / 205 (1.46%)
occurrences (all)	1	2	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 201 (0.00%)	0 / 199 (0.00%)	5 / 205 (2.44%)
occurrences (all)	0	0	5
Headache			
subjects affected / exposed	2 / 201 (1.00%)	3 / 199 (1.51%)	3 / 205 (1.46%)
occurrences (all)	2	3	3
Reproductive system and breast disorders			
Retrograde ejaculation			
subjects affected / exposed	0 / 201 (0.00%)	1 / 199 (0.50%)	4 / 205 (1.95%)
occurrences (all)	0	1	4
Erectile dysfunction			
subjects affected / exposed	3 / 201 (1.49%)	0 / 199 (0.00%)	3 / 205 (1.46%)
occurrences (all)	4	0	3
Ejaculation failure			
subjects affected / exposed	1 / 201 (0.50%)	0 / 199 (0.00%)	3 / 205 (1.46%)
occurrences (all)	1	0	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 201 (1.49%)	1 / 199 (0.50%)	0 / 205 (0.00%)
occurrences (all)	3	1	0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 201 (0.00%)	3 / 199 (1.51%)	0 / 205 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 201 (1.49%)	2 / 199 (1.01%)	2 / 205 (0.98%)
occurrences (all)	3	2	2
Infections and infestations			

influenza subjects affected / exposed occurrences (all)	3 / 201 (1.49%) 3	1 / 199 (0.50%) 1	2 / 205 (0.98%) 2

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As for Permixon, the efficacy of the positive control Tamsulosin vs placebo was not demonstrated which makes the study non conclusive.
A high placebo effect was not minimised by the exclusion of placebo responders at the end of the run-in period.

Notes: