



Clinical trial results:

Exploratory study of L.S.E.S.r. (PERMIXON® 160 mg hard capsule) versus Tamsulosine LP activity on inflammation biomarkers in the treatment of urinary symptoms related to BPH, A multinational, multicentric, randomised, double-blind, parallel-group prospective study
Summary

EudraCT number	2011-005307-33
Trial protocol	FR ES IT PT
Global end of trial date	08 October 2013

Results information

Result version number	v1 (current)
This version publication date	14 May 2016
First version publication date	14 May 2016
Summary attachment (see zip file)	P00048 GP 4 03 (07_P00048GP403_Final_Synopsis_22oct2014.pdf)

Trial information

Trial identification

Sponsor protocol code	P00048 GP 4 03
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01604811
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PIERRE FABRE MEDICAMENT
Sponsor organisation address	Centre de Recherche et Développement, 3 avenue Hubert Curien, Toulouse, France, 31035
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 October 2013
Global end of trial reached?	Yes
Global end of trial date	08 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of L.S.E.S.r. 160 mg b.i.d. and Tamsulosine LP 0.4 mg o.a.d. at D30 and D90 on biomarkers of inflammation in patients suffering from BPH :

- Urine inflammation markers on the first urine flow : gene (mRNA) expression profile of inflammation in BPH
- Serum inflammation markers : CRP and Sedimentation Rate

Protection of trial subjects:

The trial was conducted according to Good Clinical Practice (CPMP/ICH/135/95), the Declaration of Helsinki and its subsequent amendments thereto and local legal regulations. The study protocol and the informed consent form were submitted for approval to Ethics Committees before the study set up according to the national regulations.

The patient underwent a health assessment at the start of the study and remained under regular medical control during the whole study. If necessary according to investigator's opinion, the patient may be asked to attend an unscheduled visit.

During the course of the study all patients received an active treatment approved in moderate micturition disorders related to benign prostatic hyperplasia, Permixon® 160 mg hard capsules or Tamsulosine LP. A run-in period of 28 to 42 days without treatment has been decided to have reliable baseline, which is not incompatible with the management of BPH disease including watchful waiting. All study procedures are usual in medical practice for BPH management.

Antibiotics, NSAIDs and corticosteroids were allowed by local route during the course of the study. However, for ethical reasons, they may be prescribed by systemic route only in the interest of the patient's health if the investigator judges it necessary and if no alternative therapeutic drugs are possible to manage patient's complaint (exp : paracetamol for pain).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2012
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	Portugal: 11
Country: Number of subjects enrolled	Spain: 42
Country: Number of subjects enrolled	France: 163
Country: Number of subjects enrolled	Italy: 107
Worldwide total number of subjects	323
EEA total number of subjects	323

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)	150
From 65 to 84 years	172
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 42 sites were initiated in this multinational study. There were 20 centres in France, 8 centres in Italy, 3 centres in Portugal and 11 centres in Spain. Among them, 36 sites selected at least 1 patient, 34 sites randomised at least 1 patient. 323 patients were screened, 206 were randomized, 203 were treated.

Pre-assignment

Screening details:

Male patient between 45-85 years old,

Bothersome lower urinary tract symptoms existing for > 12 months

I-PSS ≥ 10 at selection visit (V1) and ≥ 12 at randomization visit (V2)

Serum tot PSA $\leq 4\text{ng/ml}$ or $\leq 10\text{mg/ml}$ and PSA(free)/PSA(tot) $\geq 25\%$ or negative prostate biopsy within the past 6 months prior to selection

Prostatic vol $\geq 30\text{cm}^3$ TRUS at V2

Period 1

Period 1 title	Wash-out / run-in period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Run-in period
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Arm description:

3 of these patients were randomised in the Tamsulosine group but not treated.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Run-in period
Started	323
Completed	203
Not completed	120
Not eligible	81
Other	11
Patient's decision	28

Period 2

Period 2 title	90-day treatment period FAS
Is this the baseline period?	Yes ^[1]
Allocation method	Randomised - controlled
Blinding used	Double blind

Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject
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Arms

Are arms mutually exclusive?	Yes
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Arm title	Permixon® 160 mg
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Permixon® 160 mg
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule, hard
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Routes of administration	Oral use
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Dosage and administration details:

1 hard capsule (160 mg) twice daily

Investigational medicinal product name	Placebo matching Tamsulosine
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

1 capsule daily

Arm title	Tamsulosine
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Arm description: -

Arm type	Active comparator
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Investigational medicinal product name	Tamsulosine
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

1 capsule (0.4 mg) daily

Investigational medicinal product name	Placebo matching Permixon®160 mg
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule, hard
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Routes of administration	Oral use
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Dosage and administration details:

1 hard capsule twice daily

Notes:

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

Justification: Period 1 correspond to wash out/run in period during patients had to discontinue treatments such as NSAIDs, corticosteroids antibiotics..and perform biological analysis. Patients were randomised at V2 to either Permixon or Tamsulosine arm.

Number of subjects in period 2^[2]	Permixon® 160 mg	Tamsulosine
Started	102	101
Completed	83	86
Not completed	19	15
Knee arthroscopy	-	1
Not eligible	4	-

lack of efficacy and safety	1	-
Patient's decision	-	1
Adverse event, non-fatal	7	3
Retroviral chronic infection	1	-
Work troubles	1	-
Inclusion wrongly	-	2
IPSS score different	1	-
Change of address	1	-
Inclusion criteria not met	-	1
Lack of efficacy	2	2
Protocol deviation	1	2
Patients not treated	-	3

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: Worldwide enrolled number of patients corresponds to screened patients at V1 ie 323 patients, among them 303 were retained at selection visit and 206 were randomised (included in the study) at V2 (V2-90 days Baseline period)

Baseline characteristics

Reporting groups

Reporting group title	Permixon® 160 mg
Reporting group description: -	
Reporting group title	Tamsulosine
Reporting group description: -	

Reporting group values	Permixon® 160 mg	Tamsulosine	Total
Number of subjects	102	101	203
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	65.4	66.1	
full range (min-max)	46.7 to 83	49.4 to 88.6	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	102	101	203
Total PSA Units: Subjects			
≤4ng/ng/ml	88	87	175
]4-10] ng/ml	14	13	27
>10 ng/ml	0	1	1
IPSS Score			
The International Prostate Symptom Score (I-PSS) was assessed on Selection visit, D1, D30 and D90. It is based on 7 questions. The overall score is the sum of all the 7 questions and therefore calculated out of a total of 35 points. For the analysis, the baseline value corresponded to the overall score of the last I-PSS filled before first study drug intake.			
Units: decimal			
arithmetic mean	17.7	16.5	
full range (min-max)	11 to 28	12 to 30	-

End points

End points reporting groups

Reporting group title	Run-in period
Reporting group description: 3 of these patients were randomised in the Tamsulosine group but not treated.	
Reporting group title	Permixon® 160 mg
Reporting group description: -	
Reporting group title	Tamsulosine
Reporting group description: -	

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CCL2

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CCL2 ^[1]
End point description:	
End point type	Primary
End point timeframe: D30 (V3)	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Descriptive analysis	

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	31		
Units: Patients				
Down-regulated	13	13		
No change	4	11		
Up-regulated	18	7		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CCL2

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CCL2 ^[2]
End point description:	
End point type	Primary
End point timeframe: D90 (V4)	

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	31		
Units: Patients				
Down-regulated	17	16		
No change	9	6		
Up-regulated	11	14		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CCR7

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CCR7 ^[3]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: Patients				
Down-regulated	2	2		
No change	0	0		
Up-regulated	0	3		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CCR7

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CCR7 ^[4]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	6		
Units: Patients				
Down-regulated	1	3		
No change	1	2		
Up-regulated	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CD40LG

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CD40LG ^[5]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[6]		
Units: Patients				
Down-regulated	1			
No change	0			
Up-regulated	0			

Notes:

[6] - CD40LG was not expressed in LnCap and the Baseline could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CD40LG

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CD40LG ^[7]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[8]	1		
Units: Patients				
Down-regulated		1		
No change		0		
Up-regulated		0		

Notes:

[8] - CD40LG was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CTLA4

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CTLA4 ^[9]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[10]		
Units: Patients				
Down-regulated	1			
No change	0			
Up-regulated	0			

Notes:

[10] - CTLA4 was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CTLA4

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CTLA4 ^[11]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[12]	0 ^[13]		
Units: Patients				
Down-regulated				
No change				
Up-regulated				

Notes:

[12] - CTLA4 was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

[13] - CTLA4 was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CXCL10

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CXCL10 ^[14]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Patients				
Down-regulated	7	7		
No change	4	11		
Up-regulated	14	7		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CXCL10

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CXCL10 ^[15]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	29		
Units: Patients				
Down-regulated	10	11		
No change	8	9		
Up-regulated	11	9		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CXCL6

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CXCL6 ^[16]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	28		
Units: Patients				
Down-regulated	9	11		
No change	8	8		
Up-regulated	15	9		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CXCL6

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CXCL6 ^[17]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Patients				
Down-regulated	12	14		
No change	8	5		
Up-regulated	10	10		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: FGF2

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: FGF2 ^[18]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	17		
Units: Patients				
Down-regulated	7	8		
No change	4	5		
Up-regulated	4	4		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: FGF2

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: FGF2 ^[19]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	16		
Units: Patients				
Down-regulated	9	9		
No change	4	5		
Up-regulated	3	2		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: ICOS

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: ICOS ^[20]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	0 ^[21]		
Units: Patients				
Down-regulated	0			
No change	0			
Up-regulated	1			

Notes:

[21] - ICOS was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: ICOS

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: ICOS ^[22]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[23]	1		
Units: Patients				
Down-regulated		0		
No change		1		
Up-regulated		0		

Notes:

[23] - ICOS was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL6

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL6 ^[24]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	6		
Units: Patients				
Down-regulated	2	2		
No change	2	2		
Up-regulated	6	2		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL6

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL6 ^[25]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: Patients				
Down-regulated	5	9		
No change	0	2		
Up-regulated	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL15

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL15 ^[26]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	21		
Units: Patients				
Down-regulated	3	6		
No change	11	9		
Up-regulated	8	6		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL15

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL15 ^[27]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Patients				
Down-regulated	5	11		
No change	8	6		
Up-regulated	6	4		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL17A

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL17A ^[28]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[29]	1		
Units: Patients				
Down-regulated		1		
No change		0		
Up-regulated		0		

Notes:

[29] - IL17A was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL17A

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL17A ^[30]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[31]	1		
Units: Patients				
Down-regulated		1		
No change		0		
Up-regulated		0		

Notes:

[31] - IL17A was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: ALOX15

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: ALOX15 ^[32]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	15		
Units: Patients				
Down-regulated	6	8		
No change	6	3		
Up-regulated	8	4		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: ALOX15

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: ALOX15 ^[33]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: Patients				
Down-regulated	8	12		
No change	5	5		
Up-regulated	6	3		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: LTC4S

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: LTC4S ^[34]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	23		
Units: Patients				
Down-regulated	5	6		
No change	10	12		
Up-regulated	11	5		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: LTC4S

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: LTC4S ^[35]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	27		
Units: Patients				
Down-regulated	11	11		
No change	10	10		
Up-regulated	11	6		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: SELP

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: SELP ^[36]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[37]	0 ^[38]		
Units: Patients				
Down-regulated				
No change				
Up-regulated				

Notes:

[37] - SELP was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

[38] - SELP was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: SELP

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: SELP ^[39]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[40]	0 ^[41]		
Units: Patients				
Down-regulated				
No change				
Up-regulated				

Notes:

[40] - SELP was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

[41] - SELP was not expressed in LnCap and the Baseline efficacy criteria could not be done for it.

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTPRC

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTPRC ^[42]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Patients				
Down-regulated	10	12		
No change	5	10		
Up-regulated	17	9		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D930 (V4) compared to baseline: PTPRC

End point title	Clinical response based on fold change in urine inflammation markers at D930 (V4) compared to baseline: PTPRC ^[43]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	36		
Units: Patients				
Down-regulated	20	13		
No change	6	8		
Up-regulated	14	15		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: ALOX15B

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: ALOX15B ^[44]
End point description:	
End point type	Primary
End point timeframe: D30 (V3)	

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	61		
Units: Patients				
Down-regulated	16	8		
No change	49	41		
Up-regulated	7	12		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: ALOX15B

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: ALOX15B ^[45]
End point description:	
End point type	Primary
End point timeframe: D90 (V4)	

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	62		
Units: Patients				
Down-regulated	10	11		
No change	53	36		
Up-regulated	12	15		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CAT

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CAT ^[46]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	81		
Units: Patients				
Down-regulated	17	13		
No change	49	49		
Up-regulated	16	19		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CAT

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CAT ^[47]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: Patients				
Down-regulated	12	11		
No change	53	46		

Up-regulated	15	23		
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Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CCL5

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: CCL5 ^[48]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	20		
Units: Patients				
Down-regulated	4	11		
No change	3	5		
Up-regulated	6	4		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CCL5

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: CCL5 ^[49]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	21		
Units: Patients				
Down-regulated	10	11		
No change	4	4		
Up-regulated	3	6		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: HIF1A

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: HIF1A ^[50]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	80		
Units: Patients				
Down-regulated	19	17		
No change	44	42		
Up-regulated	21	21		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: HIF1A

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: HIF1A ^[51]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: As in an exploratory trial with no conclusive statistical interpretation, the analysis were only descriptive analysis per arm of treatment

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	79		
Units: Patients				
Down-regulated	21	12		
No change	49	42		
Up-regulated	12	25		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: MIF

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: MIF ^[52]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: As in an exploratory trial with no conclusive statistical interpretation, the analysis were only descriptive analysis per arm of treatment

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	83		
Units: Patients				
Down-regulated	10	14		
No change	56	56		
Up-regulated	20	13		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: MIF

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: MIF ^[53]
End point description:	
End point type	Primary
End point timeframe:	
D90 (V4)	

Notes:

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

Justification: As in an exploratory trial with no conclusive statistical interpretation, the analysis were only descriptive analysis per arm of treatment

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	83		
Units: Patients				
Down-regulated	9	8		
No change	56	56		
Up-regulated	17	19		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: NFKB1

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: NFKB1 ^[54]
End point description:	
End point type	Primary
End point timeframe:	
D30 (V3)	

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	69		
Units: Patients				
Down-regulated	17	17		
No change	37	43		
Up-regulated	18	9		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: NFKB1

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: NFKB1 ^[55]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	68		
Units: Patients				
Down-regulated	22	20		
No change	41	31		
Up-regulated	12	17		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTGES2

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTGES2 ^[56]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	70		
Units: Patients				
Down-regulated	13	12		
No change	46	49		

Up-regulated	16	9		
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Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PTGES2

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PTGES2 ^[57]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	69		
Units: Patients				
Down-regulated	18	14		
No change	39	42		
Up-regulated	20	13		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTGES3

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTGES3 ^[58]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	75		
Units: Patients				
Down-regulated	13	13		
No change	50	51		
Up-regulated	18	11		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PTGES3

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PTGES3 ^[59]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	79		
Units: Patients				
Down-regulated	21	12		
No change	46	46		
Up-regulated	13	21		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTGS2

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PTGS2 ^[60]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	48		
Units: Patients				
Down-regulated	20	15		
No change	17	23		
Up-regulated	12	10		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PTGS2

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PTGS2 ^[61]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	51		
Units: Patients				
Down-regulated	19	19		
No change	21	23		
Up-regulated	14	9		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: STAT3

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: STAT3 ^[62]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	74		
Units: Patients				
Down-regulated	17	11		
No change	48	46		
Up-regulated	17	17		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: STAT3

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: STAT3 ^[63]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	72		
Units: Patients				
Down-regulated	15	9		
No change	51	48		
Up-regulated	15	15		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL1B

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL1B ^[64]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	54		
Units: Patients				
Down-regulated	24	26		
No change	15	18		
Up-regulated	19	10		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL1B

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL1B ^[65]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	57		
Units: Patients				
Down-regulated	24	32		
No change	16	10		
Up-regulated	20	15		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL8

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: IL8 ^[66]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	63		
Units: Patients				
Down-regulated	33	34		
No change	12	18		
Up-regulated	28	11		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL8

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: IL8 ^[67]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	68		
Units: Patients				
Down-regulated	35	33		
No change	18	13		
Up-regulated	20	22		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PLA2G2A

End point title	Clinical response based on fold change in urine inflammation markers at D30 (V3) compared to baseline: PLA2G2A ^[68]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	70		
Units: Patients				
Down-regulated	11	14		
No change	46	45		
Up-regulated	15	11		

Statistical analyses

No statistical analyses for this end point

Primary: Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PLA2G2A

End point title	Clinical response based on fold change in urine inflammation markers at D90 (V4) compared to baseline: PLA2G2A ^[69]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	74		
Units: Patients				
Down-regulated	13	16		
No change	48	42		
Up-regulated	14	16		

Statistical analyses

No statistical analyses for this end point

Primary: CRP: change from baseline to D30 (V3)

End point title	CRP: change from baseline to D30 (V3) ^[70]
End point description:	
End point type	Primary
End point timeframe:	
D30 (V3)	

Notes:

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

Justification: As in an exploratory trial with no conclusive statistical interpretation, the analysis were only descriptive analysis per arm of treatment

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	86		
Units: Patients				
Normal to normal	73	71		
Normal to abnormal	5	5		
Abnormal to normal	6	7		
Abnormal to abnormal	7	3		

Statistical analyses

No statistical analyses for this end point

Primary: CRP: change from baseline to D90 (V4)

End point title	CRP: change from baseline to D90 (V4) ^[71]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: As in an exploratory trial with no conclusive statistical interpretation, the analysis were only descriptive analysis per arm of treatment

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	81		
Units: Patients				
Normal to normal	67	67		
Normal to abnormal	4	4		
Abnormal to normal	7	5		
Abnormal to abnormal	4	5		

Statistical analyses

No statistical analyses for this end point

Primary: Sedimentation rate at 1 hour: change from baseline to D30

End point title	Sedimentation rate at 1 hour: change from baseline to D30 ^[72]
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End point description:

End point type	Primary
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End point timeframe:

D30 (V3)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	78		
Units: Patients				
Normal to normal	63	69		
Normal to abnormal	5	3		
Abnormal to normal	4	1		
Abnormal to abnormal	10	5		

Statistical analyses

No statistical analyses for this end point

Primary: Sedimentation rate at 1 hour: from baseline to D90

End point title	Sedimentation rate at 1 hour: from baseline to D90 ^[73]
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End point description:

End point type	Primary
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End point timeframe:

D90 (V4)

Notes:

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

Justification: Descriptive analysis

End point values	Permixon® 160 mg	Tamsulosine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	73		
Units: Patients				
Normal to normal	59	62		
Normal to abnormal	4	5		
Abnormal to normal	5	1		
Abnormal to abnormal	8	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the whole duration of the trial (from the signature of the consent for one subject)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Permixon® 160 mg
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Reporting group description: -

Reporting group title	Tamsulosine
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Reporting group description: -

Reporting group title	Wash-out / Run-in period
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Reporting group description: -

Serious adverse events	Permixon® 160 mg	Tamsulosine	Wash-out / Run-in period
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 102 (1.96%)	2 / 101 (1.98%)	4 / 323 (1.24%)
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)			
Neoformation of gallbladder			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (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
B cell non-Hodgkin lymphoma			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (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
malignant ampuloma			
subjects affected / exposed	0 / 102 (0.00%)	0 / 101 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Bilateral gynecomastia			

subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 102 (0.00%)	0 / 101 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 101 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Aggravation of lumbar spinal stenosis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (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
Hernia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 101 (0.00%)	1 / 323 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Permixon® 160 mg	Tamsulosine	Wash-out / Run-in period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 102 (25.49%)	25 / 101 (24.75%)	14 / 323 (4.33%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 102 (1.96%)	0 / 101 (0.00%)	4 / 323 (1.24%)
occurrences (all)	2	0	4
Orthostatic hypotension			
subjects affected / exposed	2 / 102 (1.96%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	3	0	0
Surgical and medical procedures			

Knee arthroplasty subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	2 / 101 (1.98%) 2	1 / 323 (0.31%) 1
Asthenia subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	2 / 101 (1.98%) 2	0 / 323 (0.00%) 0
Reproductive system and breast disorders			
Erectile dysfunction subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Retrograde ejaculation subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	4 / 101 (3.96%) 4	0 / 323 (0.00%) 0
Ejaculation failure subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	2 / 101 (1.98%) 2	0 / 323 (0.00%) 0
Genital discomfort subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Testicular pain subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Libido decreased			

subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Nightmare subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Anorgasmia subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Investigations C-reactive protein subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Prostatic specific antigen increased subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Red blood cell sedimentation rate increased subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	1 / 101 (0.99%) 1	0 / 323 (0.00%) 0
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 102 (1.96%) 3	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Balance disorder subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	0 / 101 (0.00%) 0	0 / 323 (0.00%) 0
Dysaesthesia			

subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Trigeminal neuralgia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	2 / 102 (1.96%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	1 / 102 (0.98%)	1 / 101 (0.99%)	1 / 323 (0.31%)
occurrences (all)	1	1	1
Haemorrhoids			
subjects affected / exposed	1 / 102 (0.98%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Nausea			

subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 102 (0.00%)	3 / 101 (2.97%)	0 / 323 (0.00%)
occurrences (all)	0	3	0
Anal fissure			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	1 / 323 (0.31%)
occurrences (all)	0	1	1
Flatulence			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 102 (0.98%)	2 / 101 (1.98%)	0 / 323 (0.00%)
occurrences (all)	1	2	0
Dermatitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	0	1	0
Pruritus allergic			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 102 (0.98%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			

Joint swelling			
subjects affected / exposed	1 / 102 (0.98%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	1	1	0
Joint effusion			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Pubic pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 102 (0.00%)	3 / 101 (2.97%)	1 / 323 (0.31%)
occurrences (all)	0	3	1
Muscular weakness			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	0 / 323 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 102 (0.00%)	2 / 101 (1.98%)	2 / 323 (0.62%)
occurrences (all)	0	2	2
Urinary tract infection			
subjects affected / exposed	0 / 102 (0.00%)	2 / 101 (1.98%)	1 / 323 (0.31%)
occurrences (all)	0	2	1
Ear infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 101 (0.99%)	1 / 323 (0.31%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 101 (0.00%)	0 / 323 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2012	Modification of prior or concomitant treatments Clarification of wash-out period in non-inclusion criteria related to treatments and prohibited treatments sections.
29 January 2013	Addition of adverse effects linked to Tamsulosine and Permixon and of a warning regarding concomitant administration of Tamsulosine with potent CYP3A4 inhibitors in CYP2D6 poor metabolizers patients
19 June 2013	Exploration of the arachidonic acid pathway and extension of the analysis of markers with: ALOX15, ALOX15B, ALOX5, CAT, CCL5, HIF1A, LTC4S, MIF, NFKB1, PTGES2, PTGES3, PTGS2, PTPRC, SELP, STAT3

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26306400>