Clinical trial results:
An uncontrolled, open-label, titration, long-term safety (up to 12 months) and efficacy study of tamsulosin hydrochloride in children with neuropathic bladder, with a randomized pharmacokinetic sub-study investigating low, medium and high dose ranges.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2006-004423-11
Trial protocol	DE IT BE ES
Global end of trial date	30 June 2009

Results information

Result version number	v2 (current)
This version publication date	23 July 2016
First version publication date	01 August 2015
Version creation reason	• Correction of full data set Data correction due to a system error in EudraCT- Results

Trial information

Trial identification

Sponsor protocol code	527.66

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00340704
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim, +1 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim , +1 8002430127, clintriage.rdg@boehringer-ingelheim.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 October 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 June 2009
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To characterise the pharmacokinetic (PK)/ pharmacodynamic (PD) profile and evaluate the safety and efficacy of tamsulosin hydrochloride (HCL) in children with an elevated detrussor leak point pressure associated with a known neurological disorder (e.g. spinal bifida), after which long-term safety can be assessed.

This trial has 3 different Data base locks (DBL) based on three separate populations PK / PD, Group D – Denovo and Group D – 527.51 Rollover. For PK / PD population the DBL date was 18July2007, for Group D – Denovo population the DBL date was 23Jan2009 and for Group D – 527.51 Rollover population the DBL date was 11Sep2009.

The Group D-Rollover portion of Study 527.66 was terminated early based on data from placebo-controlled Study 527.51 that showed lack of efficacy, thus, caution should be used in interpreting these results due to the impact of the early termination, as well as the impact of the study design on interpretation of results by dose.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	19 April 2006
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: 5
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	India: 26
Country: Number of subjects enrolled	United States: 58

Country: Number of subjects enrolled	Mexico: 53
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	South Africa: 14
Country: Number of subjects enrolled	Ukraine: 13
Country: Number of subjects enrolled	Philippines: 51
Country: Number of subjects enrolled	Brazil: 22
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	284
EEA total number of subjects	19

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)	226
Adolescents (12-17 years)	58
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This trial has 3 different DBLs and 3 different Clinical trial reports which were prepared based on 3 separate populations PK/PD, Group D-Denovo and Group D-527.51 Rollover. Group D-Denovo includes subjects from PK Phase and additional subjects and Group D – 527.51 Rollover includes subjects who successfully completed tamsulosin HCl Study 527.51.

Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects attended specialist sites which would then ensure that they (the subjects) met all strictly implemented inclusion/exclusion criteria. Subjects were not to be randomised to trial treatment if any one of the specific entry criteria were violated.

Period 1

Period 1 title	PK sub-study (Treatment period)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open label, randomised and uncontrolled study.

Arms

Are arms mutually exclusive?	Yes
Arm title	tamsulosin - low dose level (Steady State - PK study)

Arm description:

Subjects randomized to low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In PK study, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the Leak point pressure (LPP) results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

Subjects with body weight of 12.1–25.0 kg received low dose of 0.025 mg qd (once daily), body weight of 25.1–50.0 kg received low dose of 0.05 mg qd and body weight of 50.1–100.0 kg received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.025 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride and body weight of 12.1–25.0 kg received low dose of 0.025 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride and body weight of 25.1–50.0 kg received low dose of 0.05 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride and body weight of 50.1–100.0 kg received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm title	tamsulosin - medium dose level (Steady State - PK study)

Arm description:

Subjects randomized to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In PK study, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the LPP results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

Subjects with body weight of 12.1–25.0 kg received medium dose of 0.05 mg qd, body weight of 25.1–50.0 kg received medium dose of 0.1 mg qd with and body weight of 50.1–100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 12.1–25.0 kg received medium dose of 0.05 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 25.1–50.0 kg received medium dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.2 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 50.1–100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm title	tamsulosin - high dose level (Steady State - PK study)

Arm description:

Subjects randomized to high dose level(0.004-0.008mg/kg) of tamsulosin hydrochloride,dependent on a subject's body weight.In PK study,all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight.Depending on the results of the LPP,subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy. Subjects with body weight of 12.1-25.0kg received high dose of 0.1mg qd, body weight of 25.1-50.0kg received high dose of 0.2mg qd & body weight of 50.1-100.0kg received high dose of 0.4mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.One subject randomised to high dose level was not treated. Although actual number of subjects started is 11,10 were reported to ensure consistent reporting with baseline characteristics that includes only treated subjects.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to high dose level (0.004-0.008mg/kg) of tamsulosin hydrochloride and body weight of 12.1-25.0 kg received high dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.2 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to high dose level (0.004-0.008mg/kg) of tamsulosin hydrochloride and body weight of 25.1–50.0 kg received high dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.4 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to high dose level (0.004-0.008mg/kg) of tamsulosin hydrochloride and body weight of 50.1–100.0 kg received high dose of 0.4 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Number of subjects in period 1	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)
Started	10	10	10
Completed	10	9	10
Not completed	0	1	0
Adverse event, non-fatal	-	1	-

Period 2

Period 2 title	Group D-Denovo (Treatment period)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Open-label, uncontrolled trial and dose titrated, starting at the lowest dose level based on a subject's weight, in order to establish their individual efficacious dose.

Arms

Are arms mutually exclusive?	No
Arm title	tamsulosin - low dose level (Group D-Denovo)

Arm description:

Subjects received low dose level (0.001 – 0.002 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 12.1– 25.0 kg received low dose of 0.025 mg qd, body weight of 25.1–50.0 kg received low dose of 0.05 mg qd and body weight of 50.1–100.0 kg received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.025 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects with body weight of 12.1– 25.0 kg received low dose of 0.025 mg qd of tamsulosin hydrochloride by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects with body weight of 25.1–50.0 kg received low dose of 0.05 mg qd of tamsulosin hydrochloride by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects with body weight of 50.1–100.0 kg received low dose of 0.1 mg qd of tamsulosin hydrochloride by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm title	tamsulosin - medium dose level (Group D-Denovo)

Arm description:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 9.0–12.0 kg received medium dose of 0.025 mg qd as their starting dose, body weight of 12.1-25.0 kg could have titrated to a medium dose of 0.05 mg qd, body weight of 25.1–50.0 kg could have titrated to a medium dose of 0.1 mg qd and body weight of 50.1–100.0 kg could have titrated to a medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.025 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 9.0–12.0 kg received medium dose of 0.025 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 12.1–25.0 kg received medium dose of 0.05 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 25.1–50.0 kg received medium dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.2 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 50.1–100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm title	tamsulosin - high dose level (Group D-Denovo)

Arm description:

Subjects titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the

children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 9.0-12.0 kg received high dose of 0.05 mg qd, body weight of 12.1-25.0 kg received high dose of 0.1 mg qd, body weight of 25.1-50.0 kg received high dose of 0.2 mg qd & body weight of 50.1-100.0 kg received high dose of 0.4 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 9.0–12.0 kg received high dose of 0.05 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 12.1–25.0 kg received high dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.2 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 25.1–50.0 kg received high dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.4 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 50.1–100.0 kg received high dose of 0.4 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Number of subjects in period 2	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-Denovo)
Started	29	21	37
PK Study Subjects Entered Group D-Denovo	7 [1]	5 [2]	18 [3]
Completed	27	16	30
Not completed	2	5	7
Other reason not defined above	-	-	3
Consent withdrawn by subject	-	1	3
Adverse event, non-fatal	2	4	-
Protocol deviation	-	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Three different Clinical trial reports were prepared based on 3 separate populations (PK/PD, Group D-Denovo & Group D-527.51). Group D-Denovo includes patients from PK Phase & additional subjects. Thus this milestone represents the number of PK Study Subjects who Entered Group D-Denovo and treated for tamsulosin - low dose level.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Three different Clinical trial reports were prepared based on 3 separate populations (PK/PD, Group D-Denovo & Group D-527.51). Group D-Denovo includes patients from PK Phase & additional subjects. Thus this milestone represents the number of PK Study Subjects who Entered Group D-Denovo and treated for tamsulosin - medium dose level.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Three different Clinical trial reports were prepared based on 3 separate populations (PK/PD, Group D-Denovo & Group D-527.51). Group D-Denovo includes patients from PK Phase & additional subjects. Thus this milestone represents the number of PK Study Subjects who Entered Group D-Denovo and treated for tamsulosin - high dose level.

Period 3

Period 3 title	Group D-Rollover (Treatment period)
Is this the baseline period?	Yes[4]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	tamsulosin - low dose level (Group D-527.51 Rollover)

Arm description:

Subjects received low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D- 527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial (527.66). All subjects were to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that that the higher doses would provide some efficacy.

Subjects with body weight of 12.1-25.0 kg received low dose of 0.025 mg qd, body weight of 25.1-50.0 kg received low dose of 0.05 mg qd and body weight of 50.1-100.0 kg qd received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Arm type	Experimental

Investigational medicinal product name	tamsulosin hydrochloride (0.025 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects with body weight of 12.1– 25.0 kg received low dose of 0.025 mg qd of tamsulosin hydrochloride by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects with body weight of 25.1–50.0 kg received low dose of 0.05 mg qd of tamsulosin hydrochloride by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects with body weight of 50.1–100.0 kg received low dose of 0.1 mg qd of tamsulosin hydrochloride by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm title	tamsulosin - medium dose level (Group D-527.51 Rollover)

Arm description:

Subjects who were to receive medium dose level (0.002-0.004 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial. All subjects were to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that the higher doses would provide some efficacy.

Subjects with body weight of 9.0-12.0 kg received medium dose of 0.025 mg qd, body weight of 12.1-25.0 kg received medium dose of 0.05 mg qd , body weight of 25.1-50.0 kg received medium dose of 0.1 mg qd, body weight of 50.1-100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.025 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 9.0–12.0 kg received medium dose of 0.025 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 12.1–25.0 kg received medium dose of 0.05 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 25.1–50.0 kg received medium dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.2 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride and body weight of 50.1–100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm title	tamsulosin - high dose level (Group D-527.51 Rollover)

Arm description:

Subjects titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial. All subjects had to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that the higher doses would provide some efficacy.

Subjects with body weight of 9.0-12.0 kg received high dose of 0.05 mg, body weight of 12.1-25.0 kg received high dose of 0.1 mg, body weight of 25.1-50.0 kg received high dose of 0.2 mg, body weight of 50.1-100.0 kg received high dose of 0.4 mg by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Arm type	Experimental
Investigational medicinal product name	tamsulosin hydrochloride (0.05 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 9.0–12.0 kg received high dose of 0.05 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.1 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 12.1–25.0 kg received high dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.2 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 25.1–50.0 kg received high dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Investigational medicinal product name	tamsulosin hydrochloride (0.4 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects who were titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride and body weight of 50.1–100.0 kg received high dose of 0.4 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Notes:

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

Justification: Three separate reports were prepared for this study evaluating 3 different populations: PK sub-study, Group D-Denovo and the Group D Rollover (included subjects who entered Study 527.66 from Study 527.51). Since period 1 evaluates only the PK sub-study population, Group D-Rollover baseline data information was selected to be used for this evaluation.

Number of subjects in period 3	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)
Started	54	13	29
Completed	1	1	0
Not completed	53	12	29
Other reason not defined above	53	11	28
Adverse event, non-fatal	-	1	1

Baseline characteristics

Reporting groups[1]	
Reporting group title	Group D-Rollover (Treatment period)
Reporting group description: -	

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on the subjects who were randomised after successfully completing the screening period and received at least one dose of the trial medication (Group D-Rollover).

Reporting group values	Group D-Rollover (Treatment period)	Total	
Number of subjects	96	96	
Age categorical Units: Subjects			
Age continuous			
Treated Set: Includes all patients who are dispensed study medication and are documented to have taken at least one dose of treatment. In this study, some of the subjects are in multiple phases: PK and Group D-Denovo. Thus, the baseline characteristics are based on the unique subject entered into the study.			
Units: years			
arithmetic mean	8		
standard deviation	± 3.8	-	
Gender categorical Units: Subjects			
Female	41	41	
Male	55	55	

Subject analysis sets

Subject analysis set title	PK Study - Single dose (Treatment period)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The subject analysis type is infact Pharmacokinetics single dose set (PK-SD).

Subjects received low dose level (0.001 – 0.002 mg/kg) of tamsulosin hydrochloride once daily dependent on a subject's body weight (12.1 – 25.0 kg, 25.1 – 50.0 kg and 50.1 – 100.0 kg), by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

All subjects who were randomized, successfully took and retained the first dose of study medication and provided blood samples for PK after single dose were included in the PK-SD set.

In PK Single dose study, it was planned to obtain the Low dose PK data after single dose from all the 30 patients randomized to Low, Medium and high. However as per the protocol amendment, the PK sampling after first drug administration of low dose level was stopped after inclusion of 11 patients and therefore the PK sample of 11 patients were evaluated for PK single dose.

Subject analysis set title	PK Study - Steady state (Treatment period)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The subject analysis type is infact pharmacokinetics steady state set (PK-SS).

In PK study - steady state, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the Leak point pressure (LPP)

results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

pharmacokinetics steady state set (PK-SS): Includes all subjects who were randomized successfully took study medication for two weeks at their randomized dose level and provided blood samples for PK at their steady state visit were included in the PK-SS set.

Subject analysis set title	D-Denovo (Treatment Period)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The subject analysis type is in fact Treated set.

In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Treated set (Treat): Includes all subjects who are dispensed study medication and are documented to have taken at least one dose of treatment.

Reporting group values	PK Study - Single dose (Treatment period)	PK Study - Steady state (Treatment period)	D-Denovo (Treatment Period)
Number of subjects	11	29	87
Age categorical Units: Subjects			
Age continuous			
Treated Set: Includes all patients who are dispensed study medication and are documented to have taken at least one dose of treatment. In this study, some of the subjects are in multiple phases: PK and Group D-Denovo. Thus, the baseline characteristics are based on the unique subject entered into the study.			
Units: years			
arithmetic mean	6.5	8	7.4
standard deviation	± 4.3	± 3.8	± 3.7
Gender categorical Units: Subjects			
Female	5	13	42
Male	6	16	45

End points

End points reporting groups

Reporting group title	tamsulosin - low dose level (Steady State - PK study)

Reporting group description:

Subjects randomized to low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In PK study, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the Leak point pressure (LPP) results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

Subjects with body weight of 12.1–25.0 kg received low dose of 0.025 mg qd (once daily), body weight of 25.1–50.0 kg received low dose of 0.05 mg qd and body weight of 50.1–100.0 kg received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Reporting group title	tamsulosin - medium dose level (Steady State - PK study)

Reporting group description:

Subjects randomized to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In PK study, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the LPP results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

Subjects with body weight of 12.1–25.0 kg received medium dose of 0.05 mg qd, body weight of 25.1–50.0 kg received medium dose of 0.1 mg qd with and body weight of 50.1–100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - high dose level (Steady State - PK study)

Reporting group description:

Subjects randomized to high dose level(0.004-0.008mg/kg) of tamsulosin hydrochloride,dependent on a subject's body weight.In PK study,all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight.Depending on the results of the LPP,subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy. Subjects with body weight of 12.1-25.0kg received high dose of 0.1mg qd, body weight of 25.1-50.0kg received high dose of 0.2mg qd & body weight of 50.1-100.0kg received high dose of 0.4mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.One subject randomised to high dose level was not treated. Although actual number of subjects started is 11,10 were reported to ensure consistent reporting with baseline characteristics that includes only treated subjects.

Reporting group title	tamsulosin - low dose level (Group D-Denovo)

Reporting group description:

Subjects received low dose level (0.001 – 0.002 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 12.1– 25.0 kg received low dose of 0.025 mg qd, body weight of 25.1–50.0 kg received low dose of 0.05 mg qd and body weight of 50.1–100.0 kg received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Reporting group title	tamsulosin - medium dose level (Group D-Denovo)

Reporting group description:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 9.0–12.0 kg received medium dose of 0.025 mg qd as their starting dose, body weight of 12.1-25.0 kg could have titrated to a medium dose of 0.05 mg qd, body weight of 25.1–50.0 kg could have titrated to a medium dose of 0.1 mg qd and body weight of 50.1–100.0 kg could have titrated to a medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - high dose level (Group D-Denovo)

Reporting group description:

Subjects titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 9.0-12.0 kg received high dose of 0.05 mg qd, body weight of 12.1-25.0 kg received high dose of 0.1 mg qd, body weight of 25.1-50.0 kg received high dose of 0.2 mg qd & body weight of 50.1-100.0 kg received high dose of 0.4 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - low dose level (Group D-527.51 Rollover)

Reporting group description:

Subjects received low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D- 527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial (527.66). All subjects were to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that that the higher doses would provide some efficacy.

Subjects with body weight of 12.1-25.0 kg received low dose of 0.025 mg qd, body weight of 25.1-50.0 kg received low dose of 0.05 mg qd and body weight of 50.1-100.0 kg qd received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - medium dose level (Group D-527.51 Rollover)

Reporting group description:

Subjects who were to receive medium dose level (0.002-0.004 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial. All subjects were to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that the higher doses would provide some efficacy.

Subjects with body weight of 9.0-12.0 kg received medium dose of 0.025 mg qd, body weight of 12.1-25.0 kg received medium dose of 0.05 mg qd , body weight of 25.1-50.0 kg received medium dose of 0.1 mg qd, body weight of 50.1-100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Reporting group title	tamsulosin - high dose level (Group D-527.51 Rollover)

Reporting group description:

Subjects titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial. All subjects had to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that the higher doses would provide some efficacy.

Subjects with body weight of 9.0-12.0 kg received high dose of 0.05 mg, body weight of 12.1-25.0 kg received high dose of 0.1 mg, body weight of 25.1-50.0 kg received high dose of 0.2 mg, body weight of 50.1-100.0 kg received high dose of 0.4 mg by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Subject analysis set title	PK Study - Single dose (Treatment period)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The subject analysis type is infact Pharmacokinetics single dose set (PK-SD).

Subjects received low dose level (0.001 – 0.002 mg/kg) of tamsulosin hydrochloride once daily dependent on a subject's body weight (12.1 – 25.0 kg, 25.1 – 50.0 kg and 50.1 – 100.0 kg), by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

All subjects who were randomized, successfully took and retained the first dose of study medication and provided blood samples for PK after single dose were included in the PK-SD set.

In PK Single dose study, it was planned to obtain the Low dose PK data after single dose from all the 30 patients randomized to Low, Medium and high. However as per the protocol amendment, the PK sampling after first drug administration of low dose level was stopped after inclusion of 11 patients and therefore the PK sample of 11 patients were evaluated for PK single dose.

Subject analysis set title	PK Study - Steady state (Treatment period)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The subject analysis type is infact pharmacokinetics steady state set (PK-SS).

In PK study - steady state, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the Leak point pressure (LPP) results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

pharmacokinetics steady state set (PK-SS): Includes all subjects who were randomized successfully took study medication for two weeks at their randomized dose level and provided blood samples for PK at their steady state visit were included in the PK-SS set.

Subject analysis set title	D-Denovo (Treatment Period)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The subject analysis type is in fact Treated set.

In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Treated set (Treat): Includes all subjects who are dispensed study medication and are documented to have taken at least one dose of treatment.

Primary: Percentage of LLP responders for Group D-Denovo and Group D-527.51 Rollover

End point title	Percentage of LLP responders for Group D-Denovo and Group D-527.51 Rollover[1]

End point description:

Group D-Denovo: Leak point pressure (LPP) Response at (response defined as a subject who achieves an LPP pressure <40 cm H2O) end of treatment based on two confirmatory values. Group D-527.51 Rollover: Leak point pressure (LPP) Response at (response defined as a subject who achieves an LPP pressure <40 cm H2O) last value of the treatment based on two confirmatory values. The last value on

treatment included any final value prior to discontinuation of treatment,regardless of the length of treatment. Detrusor leak point pressure (LPP) recorded in cm H2O which was obtained using a standard urodynamic technique,a cystometrogram. Descriptive statistics were used to assess this endpoint.This Outcome Measure was only prespecified for Group D-Denovo & Group D-527.51 Rollover subjects,so results of these two groups are provided. Full Analysis Set for LPP (FAS-LPP): This subject set includes all subjects in Treated set who received one dose of treatment & had one on treatment LPP measurement.

End point type	Primary

End point timeframe:

Group D-Denovo: Week 52.
Group D-527.51 Rollover: Week 1, Week 2, Week 3 and Week 4 prior to dose administration and Week 9 (optional), Week 13 (additional), Week 26 (optional) and Week 52 after drug administration.

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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis test was tested.

End point values	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-527.51 Rollover)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26[2]	53[3]	14[4]	12[5]
Units: percentage of responders				
number (not applicable)	73.1	67.9	35.7	58.3

Notes:

[2] - FAS-LPP

[3] - FAS-LPP

[4] - FAS-LPP

[5] - FAS-LPP

End point values	tamsulosin - high dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-527.51 Rollover)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30[6]	29[7]		
Units: percentage of responders				
number (not applicable)	26.7	20.7		

Notes:

[6] - FAS-LPP

[7] - FAS-LPP

Statistical analyses

No statistical analyses for this end point

Primary: Number of LPP responders at each visit over time (classified by last value on treatment) for Group D-527.51 Rollover

End point title	Number of LPP responders at each visit over time (classified by last value on treatment) for Group D-527.51 Rollover[8]

End point description:

Number of Leak point pressure (LPP) Responders at each visit (week) over time (classified by last value on treatment).

Due to the early termination of the study, most of the LPP assessments were conducted within Weeks 1-9 of treatment. Summary of LPP response rates provided over time.The subjects are classified according to the treatment they were receiving at the last value on treatment. Therefore, no assumptions can be made regarding what dose they were receiving at a particular time point.

LD: Low dose; MD: Medium dose; HD: High dose. This Outcome Measure was only pre-specified for Group D-527.51 Rollover subjects, so results of this group is provided.

End point type	Primary

End point timeframe:

Week 1 (Visit 3) , Week 2 (Visit 4) , Week 3 (Visit 5) and Week 4 (Visit 6) prior to dose administration and Week 9 (Visit 7) (optional), Week 13 (Visit 8) (additional), Week 26 (Visit 9) (optional) and Week 52 (Visit 11) after drug administration.

Notes:

[8] - 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: This endpoint was evaluated only descriptively. Thus, no statistical hypothesis test was tested.

End point values	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53[9]	12[10]	29[11]	
Units: Participants				
number (not applicable)				
Week 1 (N= 40 (LD), 12 (MD), 27 (HD))	38	1	0	
Week 2 (N= 2 (LD), 7 (MD), 27 (HD))	2	7	2	
Week 3 (N= 3 (LD), 0 (MD), 22 (HD))	2	0	5	
Week 4 (N= 1 (LD), 0 (MD), 3 (HD))	1	0	0	
Week 9 (N= 7 (LD), 2 (MD), 16 (HD))	5	2	5	
Week 13 (N= 4 (LD), 0 (MD), 2 (HD))	1	0	1	
Week 26 (N= 2 (LD), 0 (MD), 3 (HD))	1	0	1	
Week 52 (N= 1 (LD), 1 (MD), 0 (HD))	1	1	0	

Notes:

[9] - FAS-LPP

[10] - FAS-LPP

[11] - FAS-LPP

Statistical analyses

No statistical analyses for this end point

Secondary: Early responders who maintained their LPP below 40 cm H2O during the study for Group D-Denovo and Group D-527.51 Rollover

End point title	Early responders who maintained their LPP below 40 cm H2O during the study for Group D-Denovo and Group D-527.51 Rollover

End point description:

Early responders who maintained their detrusor LPP below 40 cm H2O during the study.

Timeframe for Group D-Denovo: Low dose: Week (wk) 1, 3 & 4 prior to dose and Week 2, 9 & 26 (optional), 13(additional) & 52 post dose. Medium dose: Week 1, 2 & 4 prior to dose and Week 3, 9(optional), 13(additional), 26 (optional) & 52 post dose. High dose: Week 1, 2 & 3 prior to dose administration and Week 4, 9(optional), 13(additional), 26 (optional) & 52 post dose. Group D-527.51 Rollover: Week 1, 2, 3 & 4 prior to dose and Week 9 &26 (optional),13 (additional) & 52 post dose. This Outcome Measure was only pre-specified for Group D-Denovo and Group D-527.51 Rollover subjects, However this endpoint was analysed for the Group D-Denovo and it was not analysed for Group D-

527.51 Rollover as very limited data were collected due to the early termination of the study and no alternative endpoint was also defined in the Group D-527.51 rollover, so only the results for Group D-Denovo is provided.

End point type	Secondary

End point timeframe:

Week 1 to Week 52 (Time frame for all weeks are described study wise in the Description).

End point values	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-527.51 Rollover)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[12]	0[13]	21[14]	0[15]
Units: Participants				
number (not applicable)	17		5	

Notes:

[12] - FAS-LPP

[13] - This endpoint was not analysed due to insufficient data so no results have been analysed.

[14] - FAS-LPP

[15] - This endpoint was not analysed due to insufficient data so no results have been analysed.

End point values	tamsulosin - high dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-527.51 Rollover)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[16]	0[17]		
Units: Participants				
number (not applicable)	3			

Notes:

[16] - FAS-LPP

[17] - This endpoint was not analysed due to insufficient data so no results have been analysed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in LPP for Group D-527.51 Rollover

End point title	Change from baseline in LPP for Group D-527.51 Rollover

End point description:

Median change from baseline in detrusor leak point pressure (LPP) by treatment group (subjects are classified according to the treatment they were taking at end of treatment (EOT)) and week.

Baseline assessments were obtained from trial 527.51 for Group D-527.51 Rollover. The results from Week 1 were reported because there were very few subjects who reported data at subsequent visits due to the termination of the trial. This Outcome Measure (OM) was only pre-specified for Group D-527.51 Rollover subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

Baseline and week 1

End point values	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53[18]	12[19]	29[20]	
Units: cm H2O				
median (standard deviation)				
Baseline (N= 53 (LD), 12 (MD), 29 (HD))	48.5 (± 14.47)	48.5 (± 11.19)	55.5 (± 24.52)	
Week 1 - Actual (N= 39 (LD), 9 (MD), 22 (HD))	29 (± 8.5)	49.5 (± 8.3)	64.75 (± 27.2)	
Week 1 - Change (N= 39 (LD), 9 (MD), 22 (HD))	-25.5 (± 15.18)	-2 (± 13.68)	-1.25 (± 24.97)	

Notes:

[18] - FAS-LPP

[19] - FAS-LPP

[20] - FAS-LPP

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in LPP for Group D-527.51 Rollover

End point title	Percent change from baseline in LPP for Group D-527.51 Rollover

End point description:

Percent change from baseline in actual detrusor leak point pressure (LPP) by treatment group (subjects are classified according to the treatment they were taking at end of treatment) and Week.

Baseline assessments were obtained from trial 527.51 for Group D-527.51 Rollover.The results from Week 1 were reported because there were very few subjects who reported data at subsequent visits due to the termination of the trial. This Outcome Measure was only pre-specified for Group D-527.51 Rollover subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

Baseline and Week 1

End point values	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53[21]	12[22]	29[23]	
Units: percent change				
median (standard deviation)				
Baseline (N= 53 (LD), 12 (MD), 29 (HD))	48.5 (± 14.47)	48.5 (± 11.19)	55.5 (± 24.52)	

Week 1 - Actual (N= 39 (LD), 9 (MD), 22 (HD))	29 (± 8.5)	49.5 (± 8.3)	64.75 (± 27.2)	
Week 1 - Change (N= 39 (LD), 9 (MD), 22 (HD))	-48.48 (± 18.65)	-3.88 (± 22.43)	-2.71 (± 40.41)	

Notes:

[21] - FAS-LPP

[22] - FAS-LPP

[23] - FAS-LPP

Statistical analyses

No statistical analyses for this end point

Secondary: Response defined as stabilization or improvement of hydroureter measured by renal ultrasound compared to baseline for Group D-Denovo and Group D-527.51 Rollover

End point title	Response defined as stabilization or improvement of hydroureter measured by renal ultrasound compared to baseline for Group D-Denovo and Group D-527.51 Rollover

End point description:

Response defined as stabilization or improvement of hydroureter measured by renal ultrasound compared to baseline by treatment group(subjects classified according to treatment they were taking at wk 52 or EOT)at wk 52 for Group D-Denovo&(subjects classified according to treatment they were taking at EOT) at LVOT for Group D-527.51Rollover.Baseline assessments were obtained from trial 527.51 for Group D-527.51Rollover.The overall treatment duration was not sufficient to reach any meaningful conclusions regarding improvement or stabilization of hydroureter in Group D-527.51Rollover.Hydroureter response is defined as improvement or stabilization based upon the presence or absence of hydroureter at EOTcompared to baseline.This OM was only pre-specified for Group D-Denovo&Group D-527.51Rollover subjects,so results of these two groups are provided.
FAS for Renal (FAS-RENAL): Includes all patients in the Treated set who received one dose of treatment and had one treatment renal measurement.

End point type	Secondary

End point timeframe:

Group D-Denovo: Baseline and Week 52
Group D-527.51 Rollover: Baseline, Week 26 and Week 52.

End point values	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-527.51 Rollover)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[24]	44[25]	17[26]	8[27]
Units: Participants				
Right Kidney	26	43	15	8
Left Kidney	24	43	14	8

Notes:

[24] - FAS-RENAL

[25] - FAS-RENAL

[26] - FAS-RENAL

[27] - FAS-RENAL

End point values	tamsulosin - high dose level (Group D-	tamsulosin - high dose level (Group D-		

	Denovo)	527.51 Rollover)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[28]	19[29]		
Units: Participants				
Right Kidney	28	19		
Left Kidney	29	17		

Notes:

[28] - FAS-RENAL

[29] - FAS-RENAL

Statistical analyses

No statistical analyses for this end point

Secondary: Response defined as stabilization or improvement of hydronephrosis measured by renal ultrasound compared to baseline for Group D-Denovo and Group D-527.51 Rollover

End point title	Response defined as stabilization or improvement of hydronephrosis measured by renal ultrasound compared to baseline for Group D-Denovo and Group D-527.51 Rollover

End point description:

Response defined as stabilization or improvement of hydronephrosis measured by renal ultrasound compared to baseline by treatment group (subjects are classified according to the treatment they were taking at wk 52 or EOT) at wk 52 for Group D-Denovo & (subjects classified according to the treatment they were taking at EOT) at last value on treatment (LVOT) for Group D-527.51Rollover.Baseline assessments were obtained from trial 527.51 for Group D-527.51Rollover.Overall treatment duration was not sufficient to reach any meaningful conclusions regarding improvement or stabilization of hydronephrosis in the Group D-527.51 ollover.Hydronephrois response is defined as improvement or stabilization based upon ultrasound grading at the end of the study.The lower or same grade at EOT compared to baseline is considered an improvement or stabilization.This Outcome Measure was only pre-specified for Group D-Denovo and Group D-527.51 Rollover subjects, so results of these two groups are provided.

End point type	Secondary

End point timeframe:

Group D-Denovo: Baseline and Week 52.
Group D-527.51 Rollover: Baseline, Week 26 and Week 52.

End point values	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-527.51 Rollover)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27[30]	44[31]	17[32]	8[33]
Units: Participants				
Right Kidney	26	39	15	8
Left Kidney	24	42	14	7

Notes:

[30] - Full analysis set (FAS-RENAL)

[31] - Full analysis set (FAS-RENAL)

[32] - Full analysis set (FAS-RENAL)

[33] - Full analysis set (FAS-RENAL)

End point values	tamsulosin - high dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-527.51 Rollover)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[34]	19[35]		
Units: Participants				
Right Kidney	28	17		
Left Kidney	26	17		

Notes:

[34] - Full analysis set (FAS-RENAL)

[35] - Full analysis set (FAS-RENAL)

Statistical analyses

No statistical analyses for this end point

Secondary: LPP response at any time during the trial for Group D-Denovo and Group D-527.51 Rollover

End point title	LPP response at any time during the trial for Group D-Denovo and Group D-527.51 Rollover

End point description:

Response rates of LPP responders (2 LPP values < 40 cm H2O) at any time during the trial by treatment group.

Timeframe for Group D-Denovo: Low dose: Week 1, 3 & 4 prior to dose and Week 2, 9 & 26 (optional), 13(additional) & 52 post dose. Medium dose: Week 1, 2 & 4 prior to dose and Week 3, 9(optional), 13(additional), 26 (optional) & 52 post dose. High dose: Week 1, 2 & 3 prior to dose administration and Week 4, 9(optional), 13(additional), 26 (optional) & 52 post dose. Group D-527.51 Rollover: Week 1, 2, 3 & 4 prior to dose and Week 9 &26 (optional),13 (additional) & 52 post dose. This Outcome Measure was only pre-specified for Group D-Denovo and Group D-527.51 Rollover subjects, so results of these two groups are provided.

End point type	Secondary

End point timeframe:

Week 1 to Week 52 (described study wise in the Description).

End point values	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-527.51 Rollover)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28[36]	53[37]	21[38]	12[39]
Units: participants	26	42	16	8

Notes:

[36] - FAS-LPP

[37] - FAS-LPP

[38] - FAS-LPP

[39] - FAS-LPP

End point values	tamsulosin - high dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-527.51		

		Rollover)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[40]	29[41]		
Units: participants	16	12		

Notes:

[40] - FAS-LPP

[41] - FAS-LPP

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Clinically Relevant Abnormalities for Physical Examination, Vital Signs/Orthostatic testing, Electorocardiogram (ECG),Laboratory Values,Urinalysis,Occurence of Adverse events & Cognitive Testing for Group D-527.51 Rollover

End point title	Number of participants with Clinically Relevant Abnormalities for Physical Examination, Vital Signs/Orthostatic testing, Electorocardiogram (ECG),Laboratory Values,Urinalysis,Occurence of Adverse events & Cognitive Testing for Group D-527.51 Rollover

End point description:

Number of participants with Clinically Relevant Abnormalities for Physical Examination, Vital Signs/Orthostatic testing, Electrocardiogram (ECG), Laboratory Values, Urinalysis, Occurence of Adverse events and Cognitive Testing.

Relevant findings or worsening of baseline conditions were reported as adverse events.Below mentioned result are the number of subjects who had the clinical relevant abnormalities for the preferred term 'Hepatic enzyme increased'. This Outcome Measure was only prespecified for Group D-527.51 Rollover subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

From first drug administration until 28 days after last study drug administration, upto 395 days

End point values	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54[42]	13[43]	29[44]	
Units: Participants				
Hepatic enzyme increased	1	0	0	

Notes:

[42] - Treated Set (TS)

[43] - Treated Set (TS)

[44] - Treated Set (TS)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Clinically Relevant Abnormalities for Physical Examination, Vital Signs/Orthostatic testing, Electorocardiogram (ECG),

Laboratory Values, Urinalysis, Occurence of Adverse events and Cognitive Testing for Group D-Denovo

End point title	Number of participants with Clinically Relevant Abnormalities for Physical Examination, Vital Signs/Orthostatic testing, Electorocardiogram (ECG), Laboratory Values, Urinalysis, Occurence of Adverse events and Cognitive Testing for Group D-Denovo

End point description:

Number of participants with Clinically Relevant Abnormalities for Physical Examination, Vital Signs/Orthostatic testing, Electrocardiogram (ECG), Laboratory Values, Urinalysis, Occurence of Adverse events and Cognitive Testing.

Relevant findings or worsening of baseline conditions were reported as adverse events.

Subjects who experienced orthostatic hypotension during orthostatic testing were reported as adverse events. This Outcome Measure was only pre-specified for Group D-Denovo, so results of this group is provided.

End point type	Secondary

End point timeframe:

From first drug administration until 28 days after last study drug administration, upto 450 days

End point values	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-Denovo)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29[45]	21[46]	37[47]	
Units: Participants				
Blood urine present	0	0	1	
Body temperature increased	0	0	1	
Orthostatic hypotension	1	3	0	

Notes:

[45] - Treated Set (TS)

[46] - Treated Set (TS)

[47] - Treated Set (TS)

Statistical analyses

No statistical analyses for this end point

Secondary: Vision Testing for Group D-527.51 Rollover

End point title	Vision Testing for Group D-527.51 Rollover

End point description:

Number of subjects with a change from baseline in visual acuity by treatment group (subjects are classified according to the treatment they were taking at end of treatment).

They were analysed based on the below mentioned category in both the Eyes:
1) No Change
2) Decrease in visual acuity
3) Increase in visual acuity
4) Missing

Missing includes subjects with no baseline exam and subjects with exam scores missing. This Outcome Measure was only pre-specified for Group D-527.51 Rollover subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

Baseline, Week 26 and Week 52

End point values	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54[48]	13[49]	29[50]	
Units: Participants				
Right Eye - No Change	32	10	12	
Right Eye - Decrease in visual acuity	5	2	4	
Right Eye - Increase in visual acuity	12	1	6	
Right Eye - Missing	5	0	7	
Left Eye - No Change	31	12	12	
Left Eye - Decrease in visual acuity	8	1	3	
Left Eye - Increase in visual acuity	10	0	7	
Left Eye - Missing	5	0	7	

Notes:

[48] - Treated Set (TS)

[49] - Treated Set (TS)

[50] - Treated Set (TS)

Statistical analyses

No statistical analyses for this end point

Secondary: Vision Testing for Group D-Denovo

End point title	Vision Testing for Group D-Denovo

End point description:

Number of subjects with a change from baseline in visual acuity by treatment group (subjects are classified according to the treatment they were taking at Week 52 or end of treatment).

They were analysed based on the below mentioned category in both the Eyes:
1) No Change
2) Decrease in visual acuity
3) Increase in visual acuity
4) Missing

Missing includes subjects with no baseline exam and subjects with exam scores missing. This Outcome Measure was only pre-specified for Group D-Denovo subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

Baseline, Week 26 and Week 52.

End point values	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-Denovo)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29[51]	21[52]	37[53]	
Units: Participants				
Right Eye (Week 26) - No Change	11	7	12	
Right Eye (Week 26) - Decrease in visual acuity	8	1	8	
Right Eye (Week 26) - Increase in visual acuity	8	4	11	
Right Eye (Week 26) - Missing	2	9	6	
Left Eye (Week 26) - No Change	11	6	19	
Left Eye (Week 26) - Decrease in visual acuity	7	1	4	
Left Eye (Week 26) - Increase in visual acuity	9	5	8	
Left Eye (Week 26) – Missing	2	9	6	
Right Eye (Week 52) - No Change	7	6	16	
Right Eye (Week 52) - Decrease in visual acuity	10	2	4	
Right Eye (Week 52) - Increase in visual acuity	11	6	12	
Right Eye (Week 52) - Missing	1	7	5	
Left Eye (Week 52) - No Change	11	5	12	
Left Eye (Week 52) - Decrease in visual acuity	6	3	6	
Left Eye (Week 52) - Increase in visual acuity	11	7	14	
Left Eye (Week 52) - Missing	1	6	5	

Notes:

[51] - Treated Set (TS)

[52] - Treated Set (TS)

[53] - Treated Set (TS)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax,1

End point title	Cmax,1

End point description:

Maximum measured concentration of the analyte in plasma following the first dose, Cmax,1.

Pharmacokinetics single dose set (PK-SD): This set includes subjects who were randomized, successfully took and retained the first dose of study medication and provided blood samples for PK at Visit 2.

This Outcome Measure was only pre-specified for PK Study- single dose group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h and 8h after the drug administration.

End point values	PK Study - Single dose (Treatment period)			
Subject group type	Subject analysis set			
Number of subjects analysed	11[54]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1.67 (± 68.8)			

Notes:

[54] - Pharmacokinetics single dose set (PK-SD)

Statistical analyses

No statistical analyses for this end point

Secondary: tmax, 1

End point title	tmax, 1

End point description:

Time from dosing to maximum measured concentration of the analyte in plasma after administration of the first dose, tmax, 1.

This Outcome Measure was only pre-specified for PK Study- single dose group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h and 8h after the drug administration.

End point values	PK Study - Single dose (Treatment period)			
Subject group type	Subject analysis set			
Number of subjects analysed	11[55]			
Units: hours				
median (full range (min-max))	6 (2 to 8)			

Notes:

[55] - Pharmacokinetics single dose set (PK-SD)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax, 1 ,DW ,norm

End point title	Cmax, 1 ,DW ,norm

End point description:

Dose- and weight-normalized Cmax,1 (Cmax,1,DW,norm).

Weight normalization of Cmax,1 was performed by dividing the respective quantities by the reciprocal of body weight in kg. This Outcome Measure was only pre-specified for PK Study- single dose group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h and 8h after the drug administration.

End point values	PK Study - Single dose (Treatment period)			
Subject group type	Subject analysis set			
Number of subjects analysed	11[56]			
Units: ng/mL/mg*kg				
geometric mean (geometric coefficient of variation)	1120 (± 67.2)			

Notes:

[56] - Pharmacokinetics single dose set (PK-SD)

Statistical analyses

No statistical analyses for this end point

Secondary: Cpre,ss

End point title	Cpre,ss

End point description:

Pre-dose concentration of the analyte in plasma at steady state immediately before administration of the next dose, Cpre,ss.

Pharmacokinetics steady state set (PK-SS): This set includes subjects who were randomized successfully took study medication for two weeks at their randomized dose level and provided blood samples for PK at their steady state visit. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9[57]	9[58]	10[59]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	0.914 (± 159)	1.83 (± 131)	4.03 (± 70.6)	

Notes:

[57] - pharmacokinetics steady state set (PK-SS)

[58] - Pharmacokinetics steady state set (PK-SS)

[59] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax,ss

End point title	Cmax,ss

End point description:

Maximum measured concentration of the analyte in plasma at steady state over a uniform dosing interval τ, Cmax,ss. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[60]	9[61]	10[62]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	2.79 (± 59.5)	5.02 (± 94.8)	14.1 (± 50.3)	

Notes:

[60] - Pharmacokinetics steady state set (PK-SS)

[61] - Pharmacokinetics steady state set (PK-SS)

[62] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

Statistical analysis title	Cmax,ss (dose proportionality)

Statistical analysis description:

Dose proportionality for Cmax,ss was explored.

Comparison groups	tamsulosin - low dose level (Steady State - PK study) v tamsulosin - medium dose level (Steady State - PK study) v tamsulosin - high dose level (Steady State - PK study)
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other[63]
Parameter estimate	Slope
Point estimate	1.0039
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6499
upper limit	1.3579
Variability estimate	Standard error of the mean
Dispersion value	0.1725

Notes:

[63] - Dose proportionality for Cmax,ss was explored based on the regression model. Based on the estimate for the slope parameter, a two sided 95% confidence interval for the slope was computed. Perfect dose proportionality would correspond to a slope of 1.

Standard error of the mean is actually standard error of the slope.

Secondary: Cmax,ss, DW, norm

End point title	Cmax,ss, DW, norm

End point description:

Dose- and weight-normalized for Cmax,ss, Cmax,ss, DW, norm.

Weight normalization of Cmax,ss was performed by dividing the respective quantities by the reciprocal of body weight in kg. This Outcome Measure was only pre-specified for PK Study steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[64]	9[65]	10[66]	
Units: ng/mL/mg*kg				
geometric mean (geometric coefficient of variation)	2040 (± 74.3)	1850 (± 85.7)	2240 (± 47.6)	

Notes:

[64] - Pharmacokinetics steady state set (PK-SS)

[65] - Pharmacokinetics steady state set (PK-SS)

[66] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin,ss

End point title	Cmin,ss

End point description:

Minimum measured concentration of the analyte in plasma at steady state over a uniform dosing interval τ, Cmin,ss. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[67]	9[68]	10[69]	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	0.747 (± 99.7)	1.52 (± 130)	4.01 (± 68.5)	

Notes:

[67] - Pharmacokinetics steady state set (PK-SS)

[68] - Pharmacokinetics steady state set (PK-SS)

[69] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: tmax,ss

End point title	tmax,ss

End point description:

Time from last dosing to maximum concentration of the analyte in plasma at steady state over a uniform dosing interval τ, tmax,ss. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[70]	9[71]	10[72]	
Units: hours				
median (full range (min-max))	5 (2.33 to 8)	5.92 (2 to 8)	5.01 (2.23 to 8)	

Notes:

[70] - Pharmacokinetics steady state set (PK-SS)

[71] - Pharmacokinetics steady state set (PK-SS)

[72] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: AUCτ,ss

End point title	AUCτ,ss

End point description:

Area under the concentration-time curve of the analyte in plasma at steady state over a uniform dosing interval τ , AUCτ,ss. This Outcome Measure was only pre-specified for PK Study- steady state group

subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[73]	9[74]	10[75]	
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)	35.8 (± 75.6)	68.2 (± 94.7)	175 (± 61)	

Notes:

[73] - Pharmacokinetics steady state set (PK-SS)

[74] - Pharmacokinetics steady state set (PK-SS)

[75] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

Statistical analysis title	AUCτ,ss (Dose proportionality)

Statistical analysis description:

Dose proportionality for AUCτ,ss was explored.

Comparison groups	tamsulosin - medium dose level (Steady State - PK study) v tamsulosin - high dose level (Steady State - PK study) v tamsulosin - low dose level (Steady State - PK study)
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other[76]
Parameter estimate	Slope
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5934
upper limit	1.3666
Variability estimate	Standard error of the mean
Dispersion value	0.1884

Notes:

[76] - Dose proportionality for AUCτ,ss was explored based on the regression model. Based on the estimate for the slope parameter, a two sided 95% confidence interval for the slope was computed. Perfect dose proportionality would correspond to a slope of 1.

Standard error of the mean is actually standard error of the slope.

Secondary: AUCτ ,ss ,DW ,norm

End point title	AUCτ ,ss ,DW ,norm

End point description:

Dose- and weight-normalized of AUCτ ,ss (AUCτ ,ss ,DW ,norm).

Weight normalization of AUCτ,ss was performed by dividing the respective quantities by the reciprocal of body weight in kg. This Outcome Measure was only pre-specified for PK Study steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[77]	9[78]	10[79]	
Units: ng*h/mL/mg*kg				
geometric mean (geometric coefficient of variation)	26100 (± 91.1)	25200 (± 82.9)	27700 (± 59.1)	

Notes:

[77] - Pharmacokinetics steady state set (PK-SS)

[78] - Pharmacokinetics steady state set (PK-SS)

[79] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: λz,ss

End point title	λz,ss

End point description:

Terminal rate constant of the analyte in plasma at steady state, λz,ss. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[80]	9[81]	10[82]	
Units: 1/hours				
geometric mean (geometric coefficient of variation)	0.0589 (± 48.1)	0.0671 (± 40.8)	0.0496 (± 31.9)	

Notes:

[80] - Pharmacokinetics steady state set (PK-SS)

[81] - Pharmacokinetics steady state set (PK-SS)

[82] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: t1/2,ss

End point title	t1/2,ss

End point description:

Terminal half-life of the analyte in plasma at steady state, t1/2,ss. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[83]	9[84]	10[85]	
Units: hours				
geometric mean (geometric coefficient of variation)	11.8 (± 48.1)	10.3 (± 40.8)	14 (± 31.9)	

Notes:

[83] - Pharmacokinetics steady state set (PK-SS)

[84] - Pharmacokinetics steady state set (PK-SS)

[85] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: MRTpo,ss

End point title	MRTpo,ss

End point description:

Mean residence time of the analyte in the body at steady state after oral administration,MRTpo,ss. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[86]	9[87]	10[88]	
Units: hours				

geometric mean (geometric coefficient of variation)	18.7 (± 50.5)	17.6 (± 35)	20.9 (± 23.6)	

Notes:

[86] - Pharmacokinetics steady state set (PK-SS)

[87] - Pharmacokinetics steady state set (PK-SS)

[88] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: CL/F,ss,W,norm

End point title	CL/F,ss,W,norm

End point description:

Weight-normalized CL/F,ss (apparent clearance of the analyte in the plasma at steady state after extravascular multiple dose administration), CL/F,ss,W,norm.

Weight-normalized CL/F,ss was calculated by dividing the respective quantities by body weight in kg. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[89]	9[90]	10[91]	
Units: L/h/kg				
geometric mean (geometric coefficient of variation)	0.0383 (± 91.1)	0.0397 (± 82.9)	0.0361 (± 59.1)	

Notes:

[89] - Pharmacokinetics steady state set (PK-SS)

[90] - Pharmacokinetics steady state set (PK-SS)

[91] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: Vz/F,ss,W,norm

End point title	Vz/F,ss,W,norm

End point description:

Weight-normalized Vz/F,ss (apparent volume of distribution during the terminal phase λz at steady state following extravascular administration), Vz/F,ss,W,norm.

Weight-normalized VzF,ss was calculated by dividing the respective quantities by body weight in kg. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results of this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h, 8h, 10h, 24h and 33h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10[92]	9[93]	10[94]	
Units: L/kg				
geometric mean (geometric coefficient of variation)	0.65 (± 83.8)	0.591 (± 103)	0.729 (± 96)	

Notes:

[92] - Pharmacokinetics steady state set (PK-SS)

[93] - Pharmacokinetics steady state set (PK-SS)

[94] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Secondary: RA,Cmax

End point title	RA,Cmax

End point description:

Accumulation ratios of tamsulosin HCl in plasma at steady state after multiple dose administration over a uniform dosing interval τ, expressed as ratio of Cmax at steady state and after single dose.

The accumulation ratio RA,Cmax was calculated as : Cmax,ss/Cmax,1. This Outcome Measure was only pre-specified for PK Study- steady state group subjects, so results from this group is provided.

End point type	Secondary

End point timeframe:

−0.25h prior to dose and 2h, 4h, 6h and 8h after the drug administration.

End point values	tamsulosin - low dose level (Steady State - PK study)			
Subject group type	Reporting group			
Number of subjects analysed	4[95]			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1.58 (± 65.2)			

Notes:

[95] - Pharmacokinetics steady state set (PK-SS)

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From first drug administration until 28 days after last study drug administration, upto 80 days (Steady State - PK study), upto 450 days (Group D-Denovo) and upto 395 days (Group D-527.51 Rollover).

Adverse event reporting additional description:

Subjects were titrated to their efficacious dose.Based on LPP results,subjects could remain on that dose if it was found to be efficacious or titrate up to their higher doses which might have provided some efficacy.Therefore some of the subjects were
counted more than once for having reported adverse events with different doses of the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	tamsulosin - low dose level (Steady State - PK study)

Reporting group description:

Subjects randomized to low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In PK study, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the Leak point pressure (LPP) results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

Subjects with body weight of 12.1–25.0 kg received low dose of 0.025 mg qd (once daily), body weight of 25.1–50.0 kg received low dose of 0.05 mg qd and body weight of 50.1–100.0 kg received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Reporting group title	tamsulosin - medium dose level (Steady State - PK study)

Reporting group description:

Subjects randomized to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In PK study, all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight. Depending on the results of the LPP results, subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.

Subjects with body weight of 12.1–25.0 kg received medium dose of 0.05 mg qd, body weight of 25.1–50.0 kg received medium dose of 0.1 mg qd with and body weight of 50.1–100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - high dose level (Steady State - PK study)

Reporting group description:

Subjects randomized to high dose level(0.004-0.008mg/kg) of tamsulosin hydrochloride,dependent on a subject's body weight.In PK study,all subjects were titrated to their randomized dose level that they needed to receive which was based on their weight.Depending on the results of the LPP,subjects could remain on that dose if it was found to be efficacious or go back to a lower efficacious dose or titrate up in hopes that the higher dose would provide some efficacy.Subjects with body weight of 12.1-25.0kg received high dose of 0.1mg qd, body weight of 25.1-50.0kg received high dose of 0.2mg qd & body weight of 50.1-100.0kg received high dose of 0.4mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.One subject randomised to high dose level was not treated.Although actual number of subjects started is 11,10 were reported to ensure consistent reporting with baseline characteristics that includes only treated subjects.

Reporting group title	tamsulosin - low dose level (Group D-Denovo)

Reporting group description:

Subjects received low dose level (0.001 – 0.002 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 12.1– 25.0 kg received low dose of 0.025 mg qd, body weight of 25.1–50.0 kg received low dose of 0.05 mg qd and body weight of 50.1–100.0 kg received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Reporting group title	tamsulosin - medium dose level (Group D-Denovo)

Reporting group description:

Subjects who were titrated to medium dose level (0.002–0.004 mg/kg) of tamsulosin hydrochloride, dependent on a subject's body weight.
In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjectsremained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 9.0–12.0 kg received medium dose of 0.025 mg qd as their starting dose, body weight of 12.1-25.0 kg could have titrated to a medium dose of 0.05 mg qd, body weight of 25.1–50.0 kg could have titrated to a medium dose of 0.1 mg qd and body weight of 50.1–100.0 kg could have titrated to a medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - high dose level (Group D-Denovo)

Reporting group description:

Subjects titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-Denovo, all subjects started the study at the Low Dose level, with the exception of the children with a body weight between 9 kg and 12 kg (they started at the Medium Dose level), and titrated up to higher dose levels on a weekly basis until an efficacious level was reached. The subjects remained on their efficacious dose level for the remainder of the study.

Subjects with body weight of 9.0-12.0 kg received high dose of 0.05 mg qd, body weight of 12.1-25.0 kg received high dose of 0.1 mg qd, body weight of 25.1-50.0 kg received high dose of 0.2 mg qd & body weight of 50.1-100.0 kg received high dose of 0.4 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - low dose level (Group D-527.51 Rollover)

Reporting group description:

Subjects received low dose level (0.001–0.002 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D- 527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial (527.66). All subjects were to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that that the higher doses would provide some efficacy.

Subjects with body weight of 12.1-25.0 kg received low dose of 0.025 mg qd, body weight of 25.1-50.0 kg received low dose of 0.05 mg qd and body weight of 50.1-100.0 kg qd received low dose of 0.1 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt, taken 30 minutes after breakfast.

Reporting group title	tamsulosin - medium dose level (Group D-527.51 Rollover)

Reporting group description:

Subjects who were to receive medium dose level (0.002-0.004 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial. All subjects were to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that the higher doses would provide some efficacy.

Subjects with body weight of 12.1-25.0 kg received low dose of 0.05 mg qd, body weight of 25.1-50.0 kg received medium dose of 0.1 mg qd, body weight of 50.1-100.0 kg received medium dose of 0.2 mg qd by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Reporting group title	tamsulosin - high dose level (Group D-527.51 Rollover)

Reporting group description:

Subjects titrated to high dose level (0.004-0.008 mg/kg) of tamsulosin hydrochloride, once daily dependent on a subject's body weight.

In Group D-527.51 Rollover, once subjects exited the double-blind trial they were rolled over into this trial. All subjects had to titrate to their efficacious dose. Doses that were available were based on subject's weight. Depending on the LPP results, subjects could remain on that dose if it was found to be efficacious or titrate up in hopes that the higher doses would provide some efficacy.

Subjects with body weight of 12.1-25.0 kg received high dose of 0.1 mg, body weight of 25.1-50.0 kg received high dose of 0.2 mg, body weight of 50.1-100.0 kg received high dose of 0.4 mg by sprinkling the content of the capsule(s) over teaspoon of apple sauce or yogurt taken 30 minutes after breakfast.

Serious adverse events	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ventriculoperitoneal shunt malfunction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (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
Congenital, familial and genetic disorders			
Tibial torsion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tethered cord syndrome			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Peritoneal cyst			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-Denovo)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 82 (2.44%)	3 / 61 (4.92%)	4 / 41 (9.76%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ventriculoperitoneal shunt malfunction			
subjects affected / exposed	1 / 82 (1.22%)	1 / 61 (1.64%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Tibial torsion			
subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tethered cord syndrome			
subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	2 / 82 (2.44%)	1 / 61 (1.64%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Peritoneal cyst			
subjects affected / exposed	1 / 82 (1.22%)	0 / 61 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 82 (0.00%)	1 / 61 (1.64%)	0 / 41 (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
Infections and infestations			
Cellulitis			

subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 82 (0.00%)	1 / 61 (1.64%)	0 / 41 (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
Gastroenteritis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	2 / 41 (4.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 93 (1.08%)	1 / 41 (2.44%)	1 / 29 (3.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ventriculoperitoneal shunt malfunction			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Tibial torsion			

subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tethered cord syndrome			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Peritoneal cyst			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 93 (0.00%)	1 / 41 (2.44%)	0 / 29 (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
Urinary tract infection			
subjects affected / exposed	0 / 93 (0.00%)	1 / 41 (2.44%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 93 (1.08%)	0 / 41 (0.00%)	0 / 29 (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: 5 %

Non-serious adverse events	tamsulosin - low dose level (Steady State - PK study)	tamsulosin - medium dose level (Steady State - PK study)	tamsulosin - high dose level (Steady State - PK study)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)	5 / 10 (50.00%)	3 / 10 (30.00%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	2	0
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Mass			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Catheter related complication			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Suprapubic pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory tract congestion			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Nervousness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Cervicitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	1 / 10 (10.00%)
occurrences (all)	2	1	1

Non-serious adverse events	tamsulosin - low dose level (Group D-Denovo)	tamsulosin - medium dose level (Group D-Denovo)	tamsulosin - high dose level (Group D-Denovo)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 82 (62.20%)	25 / 61 (40.98%)	33 / 41 (80.49%)
Investigations			
Body temperature increased			

subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 82 (1.22%)	2 / 61 (3.28%)	1 / 41 (2.44%)
occurrences (all)	1	2	1
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 82 (9.76%)	2 / 61 (3.28%)	3 / 41 (7.32%)
occurrences (all)	9	4	3
Dizziness			
subjects affected / exposed	3 / 82 (3.66%)	1 / 61 (1.64%)	1 / 41 (2.44%)
occurrences (all)	3	1	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	12 / 82 (14.63%)	3 / 61 (4.92%)	6 / 41 (14.63%)
occurrences (all)	18	4	6
Mass			
subjects affected / exposed	1 / 82 (1.22%)	0 / 61 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Catheter related complication			
subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Suprapubic pain			
subjects affected / exposed	0 / 82 (0.00%)	0 / 61 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 82 (4.88%)	0 / 61 (0.00%)	1 / 41 (2.44%)
occurrences (all)	4	0	1
Abdominal pain upper			
subjects affected / exposed	3 / 82 (3.66%)	1 / 61 (1.64%)	1 / 41 (2.44%)
occurrences (all)	3	1	1
Diarrhoea			
subjects affected / exposed	4 / 82 (4.88%)	2 / 61 (3.28%)	2 / 41 (4.88%)
occurrences (all)	5	2	2

Vomiting			
subjects affected / exposed	9 / 82 (10.98%)	4 / 61 (6.56%)	3 / 41 (7.32%)
occurrences (all)	9	10	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 82 (8.54%)	1 / 61 (1.64%)	3 / 41 (7.32%)
occurrences (all)	8	1	4
Oropharyngeal pain			
subjects affected / exposed	3 / 82 (3.66%)	0 / 61 (0.00%)	1 / 41 (2.44%)
occurrences (all)	3	0	1
Respiratory tract congestion			
subjects affected / exposed	1 / 82 (1.22%)	0 / 61 (0.00%)	0 / 41 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 82 (1.22%)	2 / 61 (3.28%)	0 / 41 (0.00%)
occurrences (all)	1	2	0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	2 / 82 (2.44%)	1 / 61 (1.64%)	3 / 41 (7.32%)
occurrences (all)	2	1	3
Psychiatric disorders			
Nervousness			
subjects affected / exposed	0 / 82 (0.00%)	1 / 61 (1.64%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cervicitis			
subjects affected / exposed	1 / 82 (1.22%)	0 / 61 (0.00%)	3 / 41 (7.32%)
occurrences (all)	1	0	4
Nasopharyngitis			
subjects affected / exposed	4 / 82 (4.88%)	3 / 61 (4.92%)	1 / 41 (2.44%)
occurrences (all)	4	3	1
Influenza			
subjects affected / exposed	3 / 82 (3.66%)	1 / 61 (1.64%)	1 / 41 (2.44%)
occurrences (all)	4	1	1
Pharyngitis			

subjects affected / exposed	11 / 82 (13.41%)	1 / 61 (1.64%)	2 / 41 (4.88%)
occurrences (all)	12	1	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 82 (1.22%)	1 / 61 (1.64%)	3 / 41 (7.32%)
occurrences (all)	1	1	4
Urinary tract infection			
subjects affected / exposed	15 / 82 (18.29%)	11 / 61 (18.03%)	16 / 41 (39.02%)
occurrences (all)	18	16	23

Non-serious adverse events	tamsulosin - low dose level (Group D-527.51 Rollover)	tamsulosin - medium dose level (Group D-527.51 Rollover)	tamsulosin - high dose level (Group D-527.51 Rollover)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 93 (33.33%)	10 / 41 (24.39%)	9 / 29 (31.03%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 93 (2.15%)	1 / 41 (2.44%)	2 / 29 (6.90%)
occurrences (all)	2	1	2
Dizziness			
subjects affected / exposed	1 / 93 (1.08%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 93 (1.08%)	1 / 41 (2.44%)	1 / 29 (3.45%)
occurrences (all)	1	1	1
Mass			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Catheter related complication			

subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Suprapubic pain			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 93 (2.15%)	0 / 41 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	1
Abdominal pain upper			
subjects affected / exposed	2 / 93 (2.15%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	1 / 93 (1.08%)	2 / 41 (4.88%)	0 / 29 (0.00%)
occurrences (all)	2	2	0
Vomiting			
subjects affected / exposed	3 / 93 (3.23%)	2 / 41 (4.88%)	0 / 29 (0.00%)
occurrences (all)	4	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 93 (1.08%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 93 (1.08%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	1	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 93 (0.00%)	1 / 41 (2.44%)	0 / 29 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders			
Nervousness			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cervicitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	5 / 93 (5.38%)	1 / 41 (2.44%)	2 / 29 (6.90%)
occurrences (all)	6	1	3
Influenza			
subjects affected / exposed	5 / 93 (5.38%)	0 / 41 (0.00%)	0 / 29 (0.00%)
occurrences (all)	6	0	0
Pharyngitis			
subjects affected / exposed	2 / 93 (2.15%)	1 / 41 (2.44%)	1 / 29 (3.45%)
occurrences (all)	2	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 93 (1.08%)	1 / 41 (2.44%)	0 / 29 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	9 / 93 (9.68%)	3 / 41 (7.32%)	4 / 29 (13.79%)
occurrences (all)	16	6	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2006	1) Inclusion criteria changed to include patients up to 16 years of age (previously 15 years of age maximum) 2) Terminology "end of study" was used incorrectly and changed to "end of treatment" where applicable. 3) Additional safety monitoring was implemented, including additional ECG (Visit 9), urinalysis, and recording of post-void residual for specific visits. 4) Study population was further described as "patient with elevated detrusor leak point pressure associated with a known neurological disorder (e.g., spina bifida)". 5) Hormonal assays were added at Visit 9 for Group D-Rollover patients.
23 October 2006	1) After first 11 patients provided first-dose PK samples, first-dose PK sampling was made optional for all future patients 2) Due to altered PK sampling on Day 1 (Visit 2), vital sign testing and orthostatic testing were decreased. 3) The detrusor leak point pressure eligibility requirements were clarified 4) The addition of recent Botox injections used for urological disease management was added as an exclusion criterion. 5) Yogurt was added as an alternative drug administration vehicle, the amount of vehicle was specified, and the need to take a spoonful of water after administration of the drug was added. 6) The study drug storage conditions were further clarified

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
30 June 2009	The Group D-Rollover portion of Study 527.66 was terminated early based on data from placebo-controlled Study 527.51 that showed lack of efficacy in reducing LPP to <40 cm H2O. Reductions in detrusor LPP were observed for some patients during the study.	-

Notes:

Limitations and caveats

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

In Group D-527.51 Rollover study, due to the early termination caution should be used in interpreting these results due to the impact of the early termination, as well as the impact of the study design on interpretation of results by dose.

Notes: