

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 March 2009
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	12 February 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of a range of doses of tamsulosin hydrochloride as treatment in children with an elevated detrusor leak point pressure associated with a known neurological deficit (e.g., spina bifida).

This trial consisted two study periods:

Study Period I, double-blind, dose titration period of 2 weeks.

Study Period II, a double-blind maintenance treatment period of 3 months. In Period II, all patients completing the titration phase entered the 12-week maintenance treatment phase on their randomised dose. The patients stayed on this dose for the duration of the trial.

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	28 November 2007
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: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	India: 83
Country: Number of subjects enrolled	United States: 13
Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	Brazil: 7
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Russian Federation: 13
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 23
Country: Number of subjects enrolled	Philippines: 27
Country: Number of subjects enrolled	Ukraine: 13
Country: Number of subjects enrolled	South Africa: 16

Worldwide total number of subjects	231
EEA total number of subjects	16

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)	168
Adolescents (12-17 years)	63
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Number of subjects in period 1^[1]	Placebo	tamsulosin - low dose level	tamsulosin - medium dose level
Started	41	40	39
Completed	36	36	36
Not completed	5	4	3
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	2	-
Lost to follow-up	2	2	1
Other than stated	1	-	-
Protocol deviation	-	-	2

Number of subjects in period 1^[1]	tamsulosin - high dose level
Started	41
Completed	40
Not completed	1
Consent withdrawn by subject	1
Adverse event, non-fatal	-
Lost to follow-up	-
Other than stated	-
Protocol deviation	-

Notes:

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

Justification: Baseline characteristics are based on the patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

Age categorical			
Units: Subjects			
2 to < 5 years	8	30	
5 to < 10 years	18	70	
10 to 16 years	15	61	
Age continuous			
Treated set was used for this Study.			
Treated Set (TS): Includes all patients who were documented to have taken at least one dose of randomised treatment.			
Units: years			
arithmetic mean	8.2		
standard deviation	± 4.3	-	
Gender categorical			
Units: Subjects			
Female	16	64	
Male	25	97	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Subjects were orally administered to matching placebo to tamsulosin hydrochloride, with once daily by sprinkling the content of 2 capsules over a single teaspoonful (5 mL) of applesauce or yogurt, taken 30 minutes after meal / snack (breakfast). A teaspoonful of water was taken after ingesting the applesauce or yogurt.	
Reporting group title	tamsulosin - low dose level
Reporting group description: Subjects were orally administered to low dose level (0.001 – 0.002 mg/kg) of tamsulosin hydrochloride, once daily dependent on a patient's body weight (12.5 kg -100.0 kg), by sprinkling the content of 2 capsules over a single teaspoonful (5 mL) of applesauce or yogurt, taken 30 minutes after meal / snack (breakfast). A teaspoonful of water was taken after ingesting the applesauce or yogurt.	
Reporting group title	tamsulosin - medium dose level
Reporting group description: Subjects were orally administered to medium dose level (0.002 – 0.004 mg/kg) of tamsulosin hydrochloride, once daily dependent on a patient's body weight (12.5 kg -100.0 kg), by sprinkling the content of 2 capsules over a single teaspoonful (5 mL) of applesauce or yogurt, taken 30 minutes after meal / snack (breakfast). A teaspoonful of water was taken after ingesting the applesauce or yogurt. One subject randomised to tamsulosin - medium dose level was not treated. Although actual number of subjects started is 40, 39 were reported to ensure consistent reporting with baseline characteristics that includes only treated subjects.	
Reporting group title	tamsulosin - high dose level
Reporting group description: Subjects were orally administered to high dose level (0.004 – 0.008 mg/kg) of tamsulosin hydrochloride, once daily dependent on a patient's body weight (12.5 kg -100.0 kg), by sprinkling the content of 2 capsules over a single teaspoonful (5 mL) of applesauce or yogurt, taken 30 minutes after meal / snack (breakfast). A teaspoonful of water was taken after ingesting the applesauce or yogurt.	

Primary: Response defined as patients who decrease their detrusor leak point pressure (LPP) to <40 cm H2O based upon two evaluations on the same day.

End point title	Response defined as patients who decrease their detrusor leak point pressure (LPP) to <40 cm H2O based upon two evaluations on the same day.
End point description: The primary endpoint was response to treatment defined as patients who decreased their detrusor leak point pressure (LPP) based upon two evaluations on the same day to less than 40 cm H2O at Week 14 (end of treatment). Detrusor leak point pressure (LPP) recorded in cm H2O was obtained using a standard urodynamic technique, a cystometrogram. Full analysis set-LPP (FAS-LPP): Includes all patients in the treated set who received at least one dose of randomised. FAS-LPP contains same patients as TS. On treatment (OT): Consist of all on treatment data. Observations measured ≤ 3 days of stopping treatment was considered as on treatment. Missing data in these analyses was not replaced or imputed.	
End point type	Primary
End point timeframe: Week 14	

Comparison groups	tamsulosin - low dose level v Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4359
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.68
upper limit	11.58

Statistical analysis title	tamsulosin - medium dose vs. Placebo
Statistical analysis description: ANCOVA model was used with covariates of age group, anti-cholinergic use at baseline and geographic region. On treatment (OT) analyses approach was used.	
Comparison groups	tamsulosin - medium dose level v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0658
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.19
upper limit	37.17

Statistical analysis title	tamsulosin - high dose vs. Placebo
Statistical analysis description: ANCOVA model was used with covariates of age group, anti-cholinergic use at baseline and geographic region. On treatment (OT) analyses approach was used.	
Comparison groups	tamsulosin - high dose level v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6709
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.01
upper limit	14.87

Statistical analysis title	tamsulosin - medium dose vs. Placebo (Left Kidney)
Statistical analysis description:	
Patient responded to tamsulosin-medium dose (MD) was compared to placebo. Logistic regression model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used. The actual number of patients responded is 63 (31 in tamsulosin-MD & 32 in placebo) for Left Kidney. The pre-specified, automatically calculated number of subjects in FAS-RENAL that is provided in the statistical analysis below (78) does not reflect the actual number.	
Comparison groups	tamsulosin - medium dose level v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8724
Method	Regression, Logistic

Statistical analysis title	tamsulosin - high dose vs. Placebo (Left Kidney)
Statistical analysis description:	
Patient responded to tamsulosin-high dose (HD) was compared to placebo. Logistic regression model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used. The actual number of patients responded is 69 (37 in tamsulosin-HD & 32 in placebo) for Left Kidney. The pre-specified, automatically calculated number of subjects in FAS-RENAL that is provided in the statistical analysis below (80) does not reflect the actual number.	
Comparison groups	tamsulosin - high dose level v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7674
Method	Regression, Logistic

Statistical analysis title	tamsulosin-low dose vs. Placebo (Right Kidney)
Statistical analysis description:	
Patient responded to tamsulosin-low dose (LD) was compared to placebo. Logistic regression model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used. The actual number of patients responded is 64 (33 for tamsulosin-LD & 31 for placebo) for Right Kidney. The pre-specified, automatically calculated number of subjects in FAS-RENAL that is provided in the statistical analysis below (78) does not reflect the actual number.	
Comparison groups	tamsulosin - low dose level v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5545
Method	Regression, Logistic

Statistical analysis title	tamsulosin-medium dose vs. Placebo (Right Kidney)
Statistical analysis description:	
Patient responded to tamsulosin-Medium dose (MD) was compared to placebo. Logistic regression model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used. The actual number of patients responded is 61(30 for tamsulosin-MD & 31	

Notes:

[17] - Full analysis set-renal (FAS-RENAL), OT

[18] - Full analysis set-renal (FAS-RENAL), OT

[19] - Full analysis set-renal (FAS-RENAL), OT

[20] - Full analysis set-renal (FAS-RENAL), OT

Statistical analyses

Statistical analysis title	tamsulosin - low dose vs. Placebo (Left Kidney)
Statistical analysis description:	
Patient responded to tamsulosin-low dose (LD) was compared to placebo. Logistic regression model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used. The actual number of patients responded is 66 (33 for tamsulosin-LD & 33 for placebo) for Left Kidney. The pre-specified, automatically calculated number of subjects in FAS-RENAL that is provided in the statistical analysis below (78) does not reflect the actual number.	
Comparison groups	tamsulosin - low dose level v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9669
Method	Regression, Logistic

Statistical analysis title	tamsulosin - medium dose vs. Placebo (Left Kidney)
Statistical analysis description:	
Patient responded to tamsulosin-medium dose (MD) was compared to placebo. Logistic regression model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used. The actual number of patients responded is 65 (32 in tamsulosin-MD & 33 in placebo) for Left Kidney. The pre-specified, automatically calculated number of subjects in FAS-RENAL that is provided in the statistical analysis below (78) does not reflect the actual number.	
Comparison groups	tamsulosin - medium dose level v Placebo
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9231
Method	Regression, Logistic

Statistical analysis title	tamsulosin - high dose vs. Placebo (Left Kidney)
Statistical analysis description:	
Patient responded to tamsulosin-high dose (HD) was compared to placebo. Logistic regression model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used. The actual number of patients responded is 71 (38 in tamsulosin-HD & 33 in placebo) for Left Kidney. The pre-specified, automatically calculated number of subjects in FAS-RENAL that is provided in the statistical analysis below (80) does not reflect the actual number.	
Comparison groups	tamsulosin - high dose level v Placebo

Statistical analysis description:

ANCOVA model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used.

Comparison groups	tamsulosin - medium dose level v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.744
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.26
upper limit	47.74

Statistical analysis title

tamsulosin - high dose vs. Placebo

Statistical analysis description:

ANCOVA model was used with age group, anti-cholinergic use, and geographic region as covariates. On treatment (OT) analyses approach was used.

Comparison groups	tamsulosin - high dose level v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7703
Method	ANCOVA
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.63
upper limit	43.88

Secondary: Change from baseline in number of times patient was wet at catheterisation

End point title	Change from baseline in number of times patient was wet at catheterisation
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End point description:

Change from baseline in number of times patient was wet at time of catheterisation as recorded in catheterisation diary.

End point type	Secondary
End point timeframe:	
Baseline and Week 14.	

[30] - Treated Set (TS)

[31] - Treated Set (TS)

[32] - Treated Set (TS)

Statistical analyses

No statistical analyses for this end point

Secondary: Post void residual volume at Week 14

End point title	Post void residual volume at Week 14
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End point description:

Median change from baseline to Week 14 in post void residual (mL) by study treatment.

Treated Set (TS). Number of participants Analysed are the number of participants whose data were available for this endpoint.

End point type	Secondary
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End point timeframe:

Baseline and Week 14.

End point values	Placebo	tamsulosin - low dose level	tamsulosin - medium dose level	tamsulosin - high dose level
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31 ^[33]	36 ^[34]	34 ^[35]	38 ^[36]
Units: mL				
median (standard deviation)	3 (± 80.28)	-19 (± 66.4)	-1.5 (± 92.33)	0 (± 58.67)

Notes:

[33] - Treated Set (TS)

[34] - Treated Set (TS)

[35] - Treated Set (TS)

[36] - Treated Set (TS)

Statistical analyses

No statistical analyses for this end point

subjects affected / exposed	1 / 41 (2.44%)	0 / 120 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 41 (2.44%)	0 / 120 (0.00%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 41 (0.00%)	1 / 120 (0.83%)	0 / 80 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0

Serious adverse events	tamsulosin - high dose level		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Shunt malfunction			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	tamsulosin - low dose level	tamsulosin - medium dose level
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 41 (31.71%)	19 / 120 (15.83%)	14 / 80 (17.50%)
Nervous system disorders Headache subjects affected / exposed occurrences (all)	6 / 41 (14.63%) 6	1 / 120 (0.83%) 1	3 / 80 (3.75%) 3
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3 6 / 41 (14.63%) 8 5 / 41 (12.20%) 5	0 / 120 (0.00%) 0 1 / 120 (0.83%) 1 2 / 120 (1.67%) 2	0 / 80 (0.00%) 0 1 / 80 (1.25%) 1 4 / 80 (5.00%) 4
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 120 (0.83%) 1	5 / 80 (6.25%) 5
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection	3 / 41 (7.32%) 3 1 / 41 (2.44%) 1	3 / 120 (2.50%) 3 5 / 120 (4.17%) 6	1 / 80 (1.25%) 1 4 / 80 (5.00%) 5

subjects affected / exposed	4 / 41 (9.76%)	8 / 120 (6.67%)	2 / 80 (2.50%)
occurrences (all)	4	10	2

Non-serious adverse events	tamsulosin - high dose level		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 40 (20.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Influenza			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	8		
Urinary tract infection			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported