Clinical trial results:
Four-Week, Open-Label, Multicenter, Randomized, Parallel-Group Study to Investigate the Pharmacokinetics, Safety, Tolerability and the Effects on Leak Point Pressure of 2 Oral Doses of Alfuzosin (0.1 mg/kg/day; 0.2 mg/kg/day) in Children and Adolescents 2 to 16 Years-of-Age with Elevated Detrusor Leak Point Pressure of Neuropathic Etiology

Summary

EudraCT number	2014-004659-30
Trial protocol	Outside EU/EEA
Global end of trial date	23 February 2007

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	14 June 2015

Trial information

Trial identification

Sponsor protocol code	PKM6270

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00629720
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi Aventis Recherche & Developpement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Aventis Recherche & Developpement, Contact-US@sanofi.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	09 March 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 February 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the pharmacokinetics (PK) of 2 doses of alfuzosin (0.1 and 0.2 mg/kg/day) given as a solution containing 0.2 mg/mL alfuzosin or as tablets containing 1.5 mg alfuzosin in children and adolescents 2 to 16 years-of-age with elevated detrusor leak point pressure (LPP) (≥40 cm H2O) of neuropathic etiology stratified into 2 age groups (2 to 7 years and 8 to 16 years).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 July 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	Serbia: 24
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	29
EEA total number of subjects	0

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)	19
Adolescents (12-17 years)	10
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 6 centers in 2 countries. A total of 45 subjects were screened between 10 July 2006 and 27 December 2006.

Pre-assignment

Screening details:

Of 45 screened subjects, 29 were randomized.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Alfuzosin 0.1 mg

Arm description:

Alfuzosin 0.1 mg/kg/day for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Alfuzosin
Investigational medicinal product code	SL770499
Other name	
Pharmaceutical forms	Tablet, Oral solution
Routes of administration	Oral use

Dosage and administration details:

Age group 2 - 7 years - alfuzosin solution 3 doses TID (thrice daily).
Age group 8 - 16 years - alfuzosin tablets 2 doses BID (twice daily).

Arm title	Alfuzosin 0.2 mg

Arm description:

Alfuzosin 0.2 mg/kg/day for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Alfuzosin
Investigational medicinal product code	SL770499
Other name	
Pharmaceutical forms	Oral solution, Tablet
Routes of administration	Oral use

Dosage and administration details:

Age group 2 - 7 years - alfuzosin solution 3 doses TID.
Age group 8 - 16 years - alfuzosin tablets 2 doses BID.

Number of subjects in period 1	Alfuzosin 0.1 mg	Alfuzosin 0.2 mg
Started	14	15
Treated	14	15
Completed	14	14
Not completed	0	1
Adverse Event	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Alfuzosin 0.1 mg
Reporting group description: Alfuzosin 0.1 mg/kg/day for 4 weeks.	
Reporting group title	Alfuzosin 0.2 mg
Reporting group description: Alfuzosin 0.2 mg/kg/day for 4 weeks.	

Reporting group values	Alfuzosin 0.1 mg	Alfuzosin 0.2 mg	Total
Number of subjects	14	15	29
Age categorical Units: Subjects			
Children (2-11 years)	7	12	19
Adolescents (12-17 years)	7	3	10
Age continuous Units: years			
arithmetic mean	8.2	7	
standard deviation	± 4.2	± 3.5	-
Gender categorical Units: Subjects			
Female	9	9	18
Male	5	6	11

End points

End points reporting groups

Reporting group title	Alfuzosin 0.1 mg
Reporting group description: Alfuzosin 0.1 mg/kg/day for 4 weeks.	
Reporting group title	Alfuzosin 0.2 mg
Reporting group description: Alfuzosin 0.2 mg/kg/day for 4 weeks.	

Primary: Alfuzosin Pharmacokinetics : Area Under The Plasma Concentration-Time Curve (AUC) from 0 up to 8 hours (AUC0-8) and AUC from 0 up to 12 hours (AUC0-12)

End point title	Alfuzosin Pharmacokinetics : Area Under The Plasma Concentration-Time Curve (AUC) from 0 up to 8 hours (AUC0-8) and AUC from 0 up to 12 hours (AUC0-12)[1]

End point description:

AUC was defined as area under the plasma concentration versus time curve extrapolated to infinity. AUC0-8 was defined as area under the curves calculated using the trapezoidal method from time zero (study medication intake) up to 8 hours (TID only). AUC 0-12 was defined as area under the curves calculated using the trapezoidal method from time zero (study medication intake) up to 12 hours (BID only).

End point type	Primary

End point timeframe:

Day 1 and Day 7

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: The purpose was to provide descriptive statistics only.

End point values	Alfuzosin 0.1 mg	Alfuzosin 0.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	15		
Units: ng.h/mL				
arithmetic mean (standard deviation)				
AUC0-8: Day 1 (n=7, 8)	33 (± 6.55)	93.7 (± 49.3)		
AUC0-8: Day 7 (n=7, 8)	35.2 (± 13.1)	123 (± 69.3)		
AUC0-12: Day 1 (n=7, 7)	24.2 (± 9.92)	50 (± 15.4)		
AUC0-12: Day 7 (n=7, 7)	56.5 (± 11.4)	82.5 (± 19.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Detrusor LPP (cmH2O) at Week 4

End point title	Change From Baseline in Detrusor LPP (cmH2O) at Week 4

End point description:

The detrusor LPP was defined as the lowest detrusor pressure at which urine leakage occurred in the absence of either a detrusor contraction or increased abdominal pressure. Analysis was carried out on modified intent-to-treat (mITT) population defined as all randomized and treated subjects who had a baseline and at least one post-baseline LPP assessment.

End point type	Secondary

End point timeframe:

Baseline, Week 4

End point values	Alfuzosin 0.1 mg	Alfuzosin 0.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	15		
Units: cm H2O				
arithmetic mean (standard deviation)	-3.3 (± 26.2)	-10.3 (± 25.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Any Treatment-Emergent Adverse Events (TEAEs)

End point description:

TEAEs were defined as AEs that developed or worsened or became serious during the on-treatment portion of the study or within 2 days following the last administration of alfuzosin. Analysis was carried out on safety population defined as all subjects who were randomized and who received at least one dose of study medication.

End point type	Secondary

End point timeframe:

Up to Week 4

End point values	Alfuzosin 0.1 mg	Alfuzosin 0.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	15		
Units: subjects				
Solution (2-7 years) (n=7, 8)	4	5		
Tablets (8-16 years) (n=7, 7)	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Week 5) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (the time from the first dose of investigational product up to 48 hours (included) after the last dose, which corresponds to 5 half-lives).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Alfuzosin 0.1 mg : Solution (2-7 years)
Reporting group description:	
Alfuzosin solution (age group 2 - -7 years) 0.1 mg/kg/day for 4 weeks.	
Reporting group title	Alfuzosin 0.1 mg : Tablets (8-16 years)
Reporting group description:	
Alfuzosin tablets (age group 8 - -16 years) 0.1 mg/kg/day for 4 weeks.	
Reporting group title	Alfuzosin 0.2 mg : Solution (2-7 years)
Reporting group description:	
Alfuzosin solution (age group 2 - -7 years) 0.2 mg/kg/day for 4 weeks.	
Reporting group title	Alfuzosin 0.2 mg : Tablets (8-16 years)
Reporting group description:	
Alfuzosin tablets (age group 8 - -16 years) 0.2 mg/kg/day for 4 weeks.	

Serious adverse events	Alfuzosin 0.1 mg : Solution (2-7 years)	Alfuzosin 0.1 mg : Tablets (8-16 years)	Alfuzosin 0.2 mg : Solution (2-7 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Alfuzosin 0.2 mg : Tablets (8-16 years)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Alfuzosin 0.1 mg : Solution (2-7 years)	Alfuzosin 0.1 mg : Tablets (8-16 years)	Alfuzosin 0.2 mg : Solution (2-7 years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	1 / 7 (14.29%)	5 / 8 (62.50%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Pharyngotonsillitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	3 / 8 (37.50%)
occurrences (all)	1	0	3
Escherichia urinary tract infection			
subjects affected / exposed	2 / 7 (28.57%)	1 / 7 (14.29%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Bronchitis acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Respiratory tract infection			

subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Alfuzosin 0.2 mg : Tablets (8-16 years)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Pharyngotonsillitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Bronchitis acute			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2006	1. To clarify and include additional explanations of the following protocol items: elevated detrusor LPP, urinary tract infection (UTI), and Tanner staging 2. To add 1 new exclusion criterion related to the study subjects' safety that was established based on new practice guidelines and treatment recommendations for children with neuropathic bladder dysfunctions 3. To better characterize UTI in this study population, considering chronicity and recurrence of the problem and symptoms, because the protocol required including the subjects with a positive dipstick test for UTI.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported