Clinical trial results:
An Open-Label, Dose-Escalating Study Of The Pharmacokinetics, Safety And Tolerability Of Fesoterodine In Pediatric Overactive Bladder Patients Aged 8-17 Years.

Summary

EudraCT number	2014-004161-24
Trial protocol	Outside EU/EEA
Global end of trial date	20 December 2010

Results information

Result version number	v1 (current)
This version publication date	30 May 2016
First version publication date	12 July 2015

Trial information

Trial identification

Sponsor protocol code	A0221066

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00857896
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	17 May 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the pharmacokinetics of 5-hydroxy-methyltolterodine (5-HMT) in pediatric overactive bladder (OAB) subjects aged 8-17 years.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 March 2009
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	United States: 21
Worldwide total number of subjects	21
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)	6
Adolescents (12-17 years)	15
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 21 subjects were enrolled in 7 centres of United States. Study started from 20 Mar 2009 and completed on 20 Dec 2010.

Period 1

Period 1 title	Baseline to Week 4
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Fesoterodine

Arm description:

Fesoterodine 4 milligram (mg) tablet from Baseline to Week 4, escalated to 8 mg tablet for Weeks 5 to 8.

Arm type	Experimental
Investigational medicinal product name	Fesoterodine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Fesoterodine 4 mg tablet was administered once daily (QD) from Baseline to Week 4.

Number of subjects in period 1	Fesoterodine
Started	21
Completed	20
Not completed	1
Consent withdrawn by subject	1

Period 2

Period 2 title	Week 5 to Week 8
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Fesoterodine

Arm description:

Fesoterodine 4 mg tablet from Baseline to Week 4, escalated to 8 mg tablet QD for Weeks 5 to 8.

Arm type	Experimental
Investigational medicinal product name	Fesoterodine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Fesoterodine 8 mg tablet QD for Weeks 5 to 8.

Number of subjects in period 2	Fesoterodine
Started	20
Completed	20

Baseline characteristics

Reporting groups	
Reporting group title	Fesoterodine
Reporting group description:	
Fesoterodine 4 milligram (mg) tablet from Baseline to Week 4, escalated to 8 mg tablet for Weeks 5 to 8.	

Reporting group values	Fesoterodine	Total	
Number of subjects	21	21	
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	13.1		
standard deviation	± 2.7	-	
Gender, Male/Female Units: subjectss			
Female	9	9	
Male	12	12	

End points

End points reporting groups

Reporting group title	Fesoterodine
Reporting group description:	
Fesoterodine 4 milligram (mg) tablet from Baseline to Week 4, escalated to 8 mg tablet for Weeks 5 to 8.	
Reporting group title	Fesoterodine
Reporting group description:	
Fesoterodine 4 mg tablet from Baseline to Week 4, escalated to 8 mg tablet QD for Weeks 5 to 8.	

Primary: Absorption Rate Constant (Ka)

End point title	Absorption Rate Constant (Ka)[1]
End point description:	
Pharmacokinetic (PK) concentration population: randomized and treated subjects who had at least 1 concentration during the study.	
End point type	Primary
End point timeframe:	
Day 28 and Day 56	

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 plasma concentration-time data were analyzed by population PK modeling to estimate the 5-HMT PK parameters, for which descriptive summary statistics such as point estimate, relative standard error and 95% confidence intervals were reported

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: 1 per hour (hr)				
arithmetic mean (confidence interval 95%)	0.44 (0.15 to 0.58)			

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (VC/F)

End point title	Apparent Volume of Distribution (VC/F)[2]
End point description:	
The volume necessary to account for the total amount of drug in the body if it were present throughout the body at the same concentration found in the blood. Estimated using non linear mixed effect modeling. PK concentration population.	
End point type	Primary
End point timeframe:	
Day 28 and Day 56	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The plasma concentration-time data were analyzed by population PK modeling to estimate the 5-HMT PK parameters, for which descriptive summary statistics such as point estimate, relative standard error and 95% confidence intervals were reported

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Liters (L)				
arithmetic mean (confidence interval 95%)	1010 (566 to 1232)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the plasma drug concentration time curve (AUC)

End point title	Area Under the plasma drug concentration time curve (AUC)[3]

End point description:

AUC is a measure of the serum concentration of the drug over time. It is used to characterize drug absorption.

End point type	Primary

End point timeframe:

Day 28 and Day 56

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The plasma concentration-time data were analyzed by population PK modeling to estimate the 5-HMT PK parameters, for which descriptive summary statistics such as point estimate, relative standard error and 95% confidence intervals were reported

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: micrograms*hour per milliliter				
arithmetic mean (standard deviation)	()			

Notes:

[4] - Not analyzed due to the limited amount of data available.

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax)[5]

End point description:

End point type	Primary

End point timeframe:

Day 28 and Day 56

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The plasma concentration-time data were analyzed by population PK modeling to estimate the 5-HMT PK parameters, for which descriptive summary statistics such as point estimate, relative standard error and 95% confidence intervals were reported

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: hours				
arithmetic mean (standard deviation)	()			

Notes:

[6] - Not analyzed due to the limited amount of data available.

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax)

End point title	Maximum Observed Plasma Concentration (Cmax)[7]

End point description:

End point type	Primary

End point timeframe:

Day 28 and Day 56

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The plasma concentration-time data were analyzed by population PK modeling to estimate the 5-HMT PK parameters, for which descriptive summary statistics such as point estimate, relative standard error and 95% confidence intervals were reported

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: micrograms per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	()			

Notes:

[8] - Not analyzed due to the limited amount of data available.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Decay Half-Life (t1/2)

End point title	Plasma Decay Half-Life (t1/2)[9]

End point description:

Plasma decay half-life is the time measured for the plasma concentration to decrease by one half.

End point type	Primary

End point timeframe:

Day 28 and Day 56

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The plasma concentration-time data were analyzed by population PK modeling to estimate the 5-HMT PK parameters, for which descriptive summary statistics such as point estimate, relative standard error and 95% confidence intervals were reported

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: hours				
arithmetic mean (standard deviation)	()			

Notes:

[10] - Not analyzed due to the limited amount of data available.

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Oral Clearance (CL/F)

End point title	Apparent Oral Clearance (CL/F)[11]

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. Clearance obtained after oral dose (apparent oral clearance) is influenced by the fraction of the dose absorbed. Clearance was estimated using non linear mixed effect modeling. Drug clearance is a quantitative measure of the rate at which a drug substance is removed from the blood. PK Concentration population.

End point type	Primary

End point timeframe:

Day 28 and Day 56

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The plasma concentration-time data were analyzed by population PK modeling to estimate the 5-HMT PK parameters, for which descriptive summary statistics such as point estimate, relative standard error and 95% confidence intervals were reported

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: L/hr				
arithmetic mean (confidence interval 95%)	86.7 (63.9 to 98.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Post-void Residual (PVR) Volume

End point title	Post-void Residual (PVR) Volume

End point description:

Volume of urine remaining in the bladder immediately after urination. Safety Population: all subjects who were known to have received study medication, n = subjects not performing clean intermittent bladder catheterization (CIC) at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, Week 8 post-dose

End point values	Fesoterodine			
Subject group type	Reporting group			
Number of subjects analysed	12[12]			
Units: mL				
median (full range (min-max))				
Baseline (n=10)	6 (0 to 65)			
Week 4 (n=12)	4 (0 to 90)			
Week 8 (n=10)	25 (0 to 70)			

Notes:

[12] - Subjects not performing CIC.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 7 days after the last dose of study drug

Adverse event reporting additional description:

The same event may appear as both an adverse event (AE) and a serious AE (SAE). An event may be categorized as serious in one subject and as nonserious in an
other subject. EU BR specific AE tables were generated separately as per EU format using latest coding.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Fesoterodine 4 mg

Reporting group description:

Fesoterodine 4 mg tablet QD anytime during the study

Reporting group title	Fesoterodine 8 mg

Reporting group description:

Fesoterodine 8 mg tablet QD anytime during the study

Serious adverse events	Fesoterodine 4 mg	Fesoterodine 8 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fesoterodine 4 mg	Fesoterodine 8 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 21 (38.10%)	13 / 20 (65.00%)	
Investigations			
Residual urine volume increased			

subjects affected / exposed	0 / 21 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Congenital, familial and genetic disorders			
Developmental hip dysplasia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Resting tremor			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			

subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Sneezing			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract congestion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Joint swelling			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			

subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Myositis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Gastroenteritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis viral			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Joint abscess			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Urinary tract infection			
subjects affected / exposed	2 / 21 (9.52%)	3 / 20 (15.00%)	
occurrences (all)	2	3	
Viral infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2009	Inclusion criteria of age was changed from 8-11 years to 8-17 years.
28 July 2010	Inclusion criteria of total body weight of greater than (>) 35 kg was changed to total body weight of >25 kg.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported