Clinical trial results:
A Multicentre, Placebo Controlled, Randomised, Double-blind, Dose Ranging Study of SVT-40776 0.05 mg, 0.1 mg, 0.2 mg, Tolterodine 4 mg and Placebo Daily Doses for 4 Weeks in Patients Suffering from Overactive Bladder Syndrome

Summary

EudraCT number	2006-001378-26
Trial protocol	DE NL CZ HU ES
Global end of trial date	12 September 2007

Results information

Result version number	v1 (current)
This version publication date	31 January 2016
First version publication date	31 January 2016

Trial information

Trial identification

Sponsor protocol code	40776ORII/05IA01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00507169
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Laboratorios SALVAT, S.A.
Sponsor organisation address	Gall, 30-36, Esplugues de Llobregat, Spain, 08950
Public contact	Medical Department, Laboratorios SALVAT, S.A., 34 933946400, clinicaltrials@salvatbiotech.com
Scientific contact	Medical Director, Laboratorios SALVAT, S.A., 34 933946470, ejimenezv@salvatbiotech.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 March 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 September 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the dose-response relationship of SVT-40776 on efficacy

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 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: 3
Country: Number of subjects enrolled	Czech Republic: 99
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Hungary: 43
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	New Zealand: 27
Country: Number of subjects enrolled	Poland: 65
Country: Number of subjects enrolled	Russian Federation: 81
Country: Number of subjects enrolled	South Africa: 60
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	448
EEA total number of subjects	249

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	308
From 65 to 84 years	140
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment period was from 18th September 2006 to 12th September 2007 (Europe, USA, South Africa, Australia and New Zealand)

Pre-assignment

Screening details:

Patients between 18 and 80 years suffering from OAB based on three cardinals symptoms (urgency with or without urge incontinence, usually accompanied by frecuency or nocturia) for at least six months prior to inclusion.

Pre-assignment period milestones

Number of subjects started	669[1]
Number of subjects completed	448

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 221

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of screening patients (pre-assignement period) were 669 but only 448 were included in period 1 (Run-in period)

Period 1

Period 1 title	Run-in period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

All patients took placebo but they were not aware about of what treatment they were recieving.

Arms

Arm title	Placebo

Arm description:

Washout period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All patients self-administered a single placebo capsule each day for fourteen consecutive days, in the morning with 200ml (a glass) of water, at least 30 minutes before the first meal.

Number of subjects in period 1	Placebo
Started	448
Completed	352
Not completed	96
Consent withdrawn by subject	6
Physician decision	4
Adverse event, non-fatal	8
Enrolment failure	67
Lost to follow-up	1
Sponsor decition	5
Protocol deviation	5

Period 2

Period 2 title	Double blind
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The patients were randomized using IVRS.
All study medication products (test and comparators) had the same packaging and labels, and the boxes in which the study medication was packaged, shipped, and dispensed were identical in appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	SVT-40776 0.2mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	SVT-40776
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Each patient self-administered a single capsule each day in the morning with 200ml (a glass) of water, at least 30 minutes before the first meal for 28 consecutive days.

Arm title	SVT-40776 0.1mg

Arm description: -

Arm type	Experimental

Investigational medicinal product name	SVT-40776
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Each patient self-administered a single capsule each day in the morning with 200ml (a glass) of water, at least 30 minutes before the first meal for 28 consecutive days.

Arm title	SVT-40776 0.05mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	SVT-40776
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Each patient self-administered a single capsule each day in the morning with 200ml (a glass) of water, at least 30 minutes before the first meal for 28 consecutive days.

Arm title	Tolterodine 4mg

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Tolterodine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Each patient self-administered a single capsule each day in the morning with 200ml (a glass) of water, at least 30 minutes before the first meal for 28 consecutive days.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Each patient self-administered a single capsule each day in the morning with 200ml (a glass) of water, at least 30 minutes before the first meal for 28 consecutive days.

Number of subjects in period 2	SVT-40776 0.2mg	SVT-40776 0.1mg	SVT-40776 0.05mg
Started	69	64	78
Completed	65	63	72
Not completed	4	1	6
Consent withdrawn by subject	2	-	-
Adverse event, non-fatal	-	-	2

Sponsor decision	2	-	2
Lost to follow-up	-	-	-
Protocol deviation	-	1	2

Number of subjects in period 2	Tolterodine 4mg	Placebo
Started	67	74
Completed	62	71
Not completed	5	3
Consent withdrawn by subject	-	1
Adverse event, non-fatal	2	-
Sponsor decision	1	1
Lost to follow-up	-	1
Protocol deviation	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Washout period	

Reporting group values	Placebo	Total	
Number of subjects	448	448	
Age categorical Units: Subjects			
Adults (18-64 years)	308	308	
From 65-84 years	140	140	
Age continuous Units: years			
median	57		
full range (min-max)	20 to 79	-	
Gender categorical Units: Subjects			
Female	369	369	
Male	79	79	

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Washout period	
Reporting group title	SVT-40776 0.2mg
Reporting group description: -	
Reporting group title	SVT-40776 0.1mg
Reporting group description: -	
Reporting group title	SVT-40776 0.05mg
Reporting group description: -	
Reporting group title	Tolterodine 4mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Change in number of micturitions per 24hours	
End point title	Change in number of micturitions per 24hours
End point description:	
End point type	Primary
End point timeframe: From baseline to the end of the double blind treatment period.	

End point values	SVT-40776 0.2mg	SVT-40776 0.1mg	SVT-40776 0.05mg	Tolterodine 4mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	63	70	64
Units: micturitions				
median (full range (min-max))	-2.638 (-10.98 to 1.74)	-2.274 (-19.78 to 10.33)	-1.903 (-10.03 to 40.86)	-2.636 (-10.06 to 6.16)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: micturitions				
median (full range (min-max))	-1.928 (-8.51 to 5.36)			

Statistical analyses

Statistical analysis title	Change in the number of micturitions

Statistical analysis description:

Change in the number of micturitions per 24h from baseline to the end of the double blind treatment period

Comparison groups	SVT-40776 0.1mg v SVT-40776 0.2mg v SVT-40776 0.05mg v Tolterodine 4mg v Placebo
Number of subjects included in analysis	332
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	ANCOVA

Notes:

[1] - A hierarchical test procedure was performed. Comparison of tolterodine with placebo was a separate analysis performed exactly as for the primary analysis, as was a last observation carried forward (LOCF) analysis (carrying forward the Visit 2 value if the Visit 3 value was missing), for all analyses.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Double blind period	
Adverse event reporting additional description:	
Related Treatment Emergent Adverse Events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups	
Reporting group title	SVT-40776 0.2mg
Reporting group description: -	
Reporting group title	SVT-40776 0.1mg
Reporting group description: -	
Reporting group title	SVT-40776 0.05mg
Reporting group description: -	
Reporting group title	Tolterodine 4mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	SVT-40776 0.2mg	SVT-40776 0.1mg	SVT-40776 0.05mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Tolterodine 4mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	SVT-40776 0.2mg	SVT-40776 0.1mg	SVT-40776 0.05mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 69 (18.84%)	6 / 64 (9.38%)	15 / 78 (19.23%)
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 69 (0.00%)	1 / 64 (1.56%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	2 / 69 (2.90%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	2	0	0
Blood potassium increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 69 (1.45%)	2 / 64 (3.13%)	0 / 78 (0.00%)
occurrences (all)	1	2	0
Headache			
subjects affected / exposed	1 / 69 (1.45%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 69 (1.45%)	1 / 64 (1.56%)	0 / 78 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eyelid oedema			
subjects affected / exposed	1 / 69 (1.45%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0

Eyelids pruritus			
subjects affected / exposed	1 / 69 (1.45%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	1 / 69 (1.45%)	1 / 64 (1.56%)	1 / 78 (1.28%)
occurrences (all)	1	1	1
Eye pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 69 (1.45%)	0 / 64 (0.00%)	1 / 78 (1.28%)
occurrences (all)	1	0	2
Dry mouth			
subjects affected / exposed	8 / 69 (11.59%)	3 / 64 (4.69%)	9 / 78 (11.54%)
occurrences (all)	8	3	10
Dyspepsia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 69 (0.00%)	1 / 64 (1.56%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	1 / 69 (1.45%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 69 (0.00%)	1 / 64 (1.56%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 69 (0.00%)	1 / 64 (1.56%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			

subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 69 (0.00%)	1 / 64 (1.56%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 69 (0.00%)	1 / 64 (1.56%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 64 (0.00%)	1 / 78 (1.28%)
occurrences (all)	0	0	1

Non-serious adverse events	Tolterodine 4mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 67 (20.90%)	24 / 74 (32.43%)	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
Blood glucose increased			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	

Blood potassium increased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 67 (2.99%)	1 / 74 (1.35%)	
occurrences (all)	2	1	
Headache			
subjects affected / exposed	2 / 67 (2.99%)	1 / 74 (1.35%)	
occurrences (all)	3	1	
Somnolence			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	1 / 67 (1.49%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Thirst			
subjects affected / exposed	0 / 67 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Eye disorders			
Eyelid oedema			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
Eyelids pruritus			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	1 / 67 (1.49%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Eye pain			
subjects affected / exposed	1 / 67 (1.49%)	0 / 74 (0.00%)	
occurrences (all)	1	0	

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 67 (0.00%)	2 / 74 (2.70%)	
occurrences (all)	0	4	
Dry mouth			
subjects affected / exposed	6 / 67 (8.96%)	5 / 74 (6.76%)	
occurrences (all)	6	5	
Dyspepsia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	1 / 67 (1.49%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 67 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Nasal dryness			
subjects affected / exposed	0 / 67 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	

Hyperhidrosis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 67 (1.49%)	0 / 74 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 67 (0.00%)	0 / 74 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2006	To clarify inclusion/exclusion criteria and procedures, and modify the storage temperature of study medication.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported