Clinical trial results:
A Double-Blind, Randomised, Placebo-Controlled, Parallel-Group, Phase 2, Dose Ranging Trial to Evaluate the Efficacy, Safety, and Tolerability of Oral Litoxetine 10mg,20mg and 40mg Twice Daily (BID) versus Placebo in Women with Mixed Urinary Incontinence

Summary

EudraCT number	2016-004307-30
Trial protocol	PL FR GB
Global end of trial date	13 March 2019

Results information

Result version number	v1 (current)
This version publication date	31 May 2019
First version publication date	31 May 2019
Summary attachment (see zip file)	CSR synopsis (IXA-CSP-001_synopsis.docx)

Trial information

Trial identification

Sponsor protocol code	IXA-CSP-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	VHP REFERENCE NUMBER: VHP-No: VHP1022 (VHP2016175)

Notes:

Sponsors

Sponsor organisation name	Ixaltis SA
Sponsor organisation address	Archamps Technopole, 60 avenue Marie Curie, Archamps, France, 74160
Public contact	Elisabeth Svanberg, Ixaltis SA, 33 457260076, svanberg@ixaltis.com
Scientific contact	Elisabeth Svanberg, Ixaltis SA, 33 457260076, svanberg@ixaltis.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	13 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 March 2019
Global end of trial reached?	Yes
Global end of trial date	13 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the effectiveness of the 3 doses of Litoxetine (10mgs,20mgs,and 40mgs taken two times per day)versus placebo (inactive substance). Female adult patients will take part with a diagnosis of Mixed Urinary Incontinence (MUI)

Protection of trial subjects:

Adherence to GCP and Declaration of Helsinki, local law and regulation, protocol and ICF approved by IRB/EC

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2017
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	Poland: 35
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Georgia: 58
Country: Number of subjects enrolled	Ukraine: 77
Worldwide total number of subjects	198
EEA total number of subjects	39

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)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	134
From 65 to 84 years	64
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment in Canada, France, Georgia, Poland, UK, Ukraine March 2017 - May 2018

Pre-assignment

Screening details:

Women age 18-75 years of age
Urinary Incontinence of at least 3 months duration

Pre-assignment period milestones

Number of subjects started	198
Number of subjects completed	198

Period 1

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

Arms

Arm title	placebo

Arm description:

placebo

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

Dosage and administration details:

10, 20 or 40 mg BID

Number of subjects in period 1	placebo
Started	198
Completed	198

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Litoxetine 10 mg BID

Arm description:
Litoxetine 10 mg BID

Arm type	Experimental
Investigational medicinal product name	Litoxetine benzoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
10 mg BID

Arm title	Litoxetine 20 mg BID

Arm description:
Litoxetine 20 mg BID

Arm type	Experimental
Investigational medicinal product name	Litoxetine benzoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
Litoxetine 20 mg BID

Arm title	Litoxetine 40 mg BID

Arm description:
Litoxetine 40 mg BID

Arm type	Experimental
Investigational medicinal product name	Litoxetine benzoate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
Litoxetine 40 mg BID

Arm title	placebo

Arm description:
Placebo

Arm type	Placebo

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
placebo BID

Number of subjects in period 2	Litoxetine 10 mg BID	Litoxetine 20 mg BID	Litoxetine 40 mg BID
Started	48	52	48
Completed	48	52	48

Number of subjects in period 2	placebo
Started	50
Completed	50

Baseline characteristics

Reporting groups	
Reporting group title	placebo
Reporting group description:	
placebo	

Reporting group values	placebo	Total	
Number of subjects	198	198	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	57		
standard deviation	± 12	-	
Gender categorical Units: Subjects			
Female	198	198	
Male	0	0	

Subject analysis sets	
Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol
Subject analysis set description:	
The 4 arms in the treatment period are used for the analysis of study data.	

Reporting group values	Per protocol population		
Number of subjects	164		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			

Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years median standard deviation	 57 ± 12		
Gender categorical Units: Subjects			
Female Male	164 0		

End points

End points reporting groups

Reporting group title	placebo
Reporting group description: placebo	
Reporting group title	Litoxetine 10 mg BID
Reporting group description: Litoxetine 10 mg BID	
Reporting group title	Litoxetine 20 mg BID
Reporting group description: Litoxetine 20 mg BID	
Reporting group title	Litoxetine 40 mg BID
Reporting group description: Litoxetine 40 mg BID	
Reporting group title	placebo
Reporting group description: Placebo	
Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol
Subject analysis set description: The 4 arms in the treatment period are used for the analysis of study data.	

Primary: Change in incontinence event frequency

End point title	Change in incontinence event frequency
End point description: Change in number of incontinence episodes/ week	
End point type	Primary
End point timeframe: 12 weeks	

End point values	Litoxetine 10 mg BID	Litoxetine 20 mg BID	Litoxetine 40 mg BID	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	45	34	46
Units: events/week				
number (confidence interval 95%)	0.51 (0.37 to 0.69)	0.52 (0.40 to 0.69)	0.38 (0.26 to 0.55)	0.49 (0.35 to 0.67)

End point values	Per protocol population			
Subject group type	Subject analysis set			
Number of subjects analysed	164			
Units: events/week				
number (confidence interval 95%)	1 (1 to 1)			

Attachments (see zip file)	Ph 2 efficacy/Litoxetine ph 2 efficacy result EudraCT.pptx

Statistical analyses

Statistical analysis title	ANCOVA
Statistical analysis description:	
Comparison was made between the 40 mg BID group and the plkacebo group, and subsequenbtly between the 20 mg BID and 10 mg BID group to placebo	
Comparison groups	Litoxetine 10 mg BID v Litoxetine 20 mg BID v Litoxetine 40 mg BID v placebo
Number of subjects included in analysis	164
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	= 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events: March 2017- October 2018	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Treatment period

Reporting group description: -

Serious adverse events	Treatment period		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 198 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.02 %

Non-serious adverse events	Treatment period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 198 (19.70%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 198 (3.54%)		
occurrences (all)	7		
General disorders and administration site conditions			
Asthenia	Additional description: The reporting includes also the term 'fatigue'		
subjects affected / exposed	5 / 198 (2.53%)		
occurrences (all)	5		
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	15 / 198 (7.58%) 16 4 / 198 (2.02%) 4 3 / 198 (1.52%) 3		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	3 / 198 (1.52%) 3		

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