Clinical trial results:
EFFECTS OF TWO DIFFERENT DOSES OF REC 0/0438 ADMINISTERED BY INTRA-VESICAL INSTILLATION IN PATIENTS WITH NEUROGENIC DETRUSOR OVERACTIVITY DUE TO SPINAL CORD INJURY: A REPEATED DOSES, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY

Summary

EudraCT number	2017-000905-19
Trial protocol	PT PL CZ FR
Global end of trial date	27 March 2019

Results information

Result version number	v1 (current)
This version publication date	10 December 2020
First version publication date	10 December 2020

Trial information

Trial identification

Sponsor protocol code	REC 0/0438-IT-CL 0491

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03482037
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Recordati SPA
Sponsor organisation address	Via Civitali, 1, Milan, Italy, 20148
Public contact	Senior Clinical Project Leader, Recordati S.p.A, 0039 02487871, casi.m@recordati.it
Scientific contact	Senior Clinical Project Leader, Recordati S.p.A, 0039 02487871, casi.m@recordati.it
Sponsor organisation name	Recordati SPA
Sponsor organisation address	Via Civitali, 1, Milan, Italy, 20148
Public contact	Massimo Casi, MD, Medical Department, Recordati SPA, casi.m@recordati.it
Scientific contact	Massimo Casi, MD, Medical Department, Recordati SPA, casi.m@recordati.it

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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 March 2020
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	27 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to investigate the safety and tolerability of repeated doses of Rec 0/0438 administered by intravesical instillation for four weeks in subjects suffering from NDO

Protection of trial subjects:

Cystometry: the procedure has been performed only by qualified and experienced operators according to international good practice guidelines and the subjects' health status has been monitored.
Blood tests: the quantity of blood taken for testing did not constitute a danger for the subjects' health.

Background therapy:

The use of placebo was considered acceptable in this study since it was administered on top of current treatment (antimuscarinic drugs).

Evidence for comparator: -

Actual start date of recruitment	07 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 37
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	France: 1
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	42
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

FPI: 07 June 2018
LPLV: 27 March 2019

Pre-assignment

Screening details:

Male or female patients aged between 18 and 65 years and suffering from NDO due to SCI at upper motor neuron level (below C6) and emptying the bladder performing clear intermittent self-catheterisation (CISC) with at least 1 incontinence episode/day, reported in the bladder diary, despite current treatment.

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Blinding implementation details:

The patients, the Investigators, the Sponsor and the statistician were kept blind. DSMC received blinded data for its analysis. The study personnel were fully blinded throughout the study and remained so until unblinding after database lock. Measures were taken to ensure that test drug/investigational product and placebo were indistinguishable in regard to appearance, shape, smell, and taste of the test material.

Arms

Are arms mutually exclusive?	Yes
Arm title	REC 0/0438 1 mg

Arm description:

REC 0/0438 1 mg

Arm type	Experimental
Investigational medicinal product name	REC 0/0438 1 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for intravesical solution
Routes of administration	Intravesical use

Dosage and administration details:

REC 0/0438 1 mg oad. The study drug was administered after voiding of the bladder at the end of the first self-catheterisation of the day

Arm title	REC 0/0438 2 mg

Arm description:

REC 0/0438 2 mg

Arm type	Experimental
Investigational medicinal product name	REC 0/0438 2 mg
Investigational medicinal product code	REC 0/0438 2 mg
Other name	
Pharmaceutical forms	Powder for intravesical solution
Routes of administration	Intravesical use

Dosage and administration details:

REC 0/0438 2 mg oad. The study drug was administered after voiding of the bladder at the end of the first self-catheterisation of the day

Arm title	Placebo

Arm description:	
Placebo	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for intravesical solution
Routes of administration	Intravesical use

Dosage and administration details:

Placebo oad. The study drug was administered after voiding of the bladder at the end of the first self-catheterisation of the day

Number of subjects in period 1	REC 0/0438 1 mg	REC 0/0438 2 mg	Placebo
Started	14	13	15
Completed	14	13	13
Not completed	0	0	2
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	42	42	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	42	42	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	38.3		
standard deviation	± 10.5	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	36	36	

End points

End points reporting groups

Reporting group title	REC 0/0438 1 mg
Reporting group description: REC 0/0438 1 mg	
Reporting group title	REC 0/0438 2 mg
Reporting group description: REC 0/0438 2 mg	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Safety and Tolerability

End point title	Safety and Tolerability[1]
End point description:	
End point type	Primary
End point timeframe: From Baseline to End of study treatment	

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: Due to the exploratory nature of the study and the small sample size, the safety data have been evaluated by means of descriptive statistics only and summarised by treatment group.

End point values	REC 0/0438 1 mg	REC 0/0438 2 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	15	
Units: Treatment Emergent AEs				
number (not applicable)	7	4	5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From baseline to end of study treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0
Reporting groups	
Reporting group title	REC 0/0438 1 mg
Reporting group description: -	
Reporting group title	REC 0/0438 2 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	REC 0/0438 1 mg	REC 0/0438 2 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 15 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 15 (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

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

Non-serious adverse events	REC 0/0438 1 mg	REC 0/0438 2 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 14 (28.57%)	4 / 13 (30.77%)	5 / 15 (33.33%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vascular disorders			

Emathoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 14 (0.00%)	1 / 13 (7.69%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Orchitis noninfective			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 14 (0.00%)	0 / 13 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Infections and infestations			
Viral pharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 13 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	2 / 14 (14.29%)	3 / 13 (23.08%)	4 / 15 (26.67%)
occurrences (all)	2	3	4

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