Clinical trial results:
A Phase IV, interventional, monocentric, not controlled study for the evaluation of new clinical and instrumental parameters on the efficacy of SOMATOLINE in the treatment of local adiposity and cellulite

Summary

EudraCT number	2020-003740-89
Trial protocol	IT
Global end of trial date	05 April 2022

Results information

Result version number	v1 (current)
This version publication date	19 April 2023
First version publication date	19 April 2023

Trial information

Trial identification

Sponsor protocol code	MR-Som-01-20

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Manetti & Roberts Spa
Sponsor organisation address	Via Baldanzese 177, Calenzani/Firenze, Italy, 50141
Public contact	Regulatory Affairs, Manetti & Roberts Spa, 0039 00390558835320, csabatini@manettiroberts.it
Scientific contact	Regulatory Affairs, Manetti & Roberts Spa, 0039 0558835320, csabatini@manettiroberts.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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 April 2022
Global end of trial reached?	Yes
Global end of trial date	05 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of SOMATOLINE in the treatment of cellulite by the reduction versus baseline of CSS score measured in the thighs at 14 and 28 days of treatment

Protection of trial subjects:

Informed consent and data privacy was signed by all the subjects. According with available safety data, the risks to patients were considered hardly distinguishable from those of placebo. The safety of the cutaneous use of SOMATOLINE rests in fact on biochemical and pharmacological bases, on results of bioavailability studies that document the lack of circulation of significant portions of levo-thyroxine, on controlled clinical studies and on pharmacovigilance data of over 40 years marketing of the product.
This study did not imply the presence of a placebo arm, so the expected benefits for the patient were considered, from the clinical point of view and for the duration of the study, substantially superimposable to those already clinically documented for SOMATOLINE, even if in the studies conducted so far, the benefits were not assessed with recent and validated rating scales.
The favorable risk / benefit ratio of SOMATOLINE, the wide knowledge of its pharmacological and therapeutic profile, the inclusion and exclusion criteria related to the protocol and the short duration of the study did not require sophisticated risk mitigation measures.
The fortnightly check-ups in the first phase of the study and the self-assessment by the patient, required by the protocol, were considered adequate to monitor and, if necessary, to take measure to control and to mitigate the critical issues and risks to which patients may be exposed.

Background therapy:

Due to the nature of the disease under study (cellulite) no background therapy was planned.

Evidence for comparator:

No comparator was used for this study

Actual start date of recruitment	22 February 2021
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	Italy: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In the period between 22/02/2021 and 14/02/2022, the Dermatology Division screened 35 women, 24 met all inclusion/excusion criteria and were enrolled

Pre-assignment

Screening details:

Out of 35 patients screened, 11 patients were screening failures. For 8 patients out of 11 (72.7%) the cause of exclusion was evidence of thyroid abnormalities or dysfunction.

Period 1

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

Arms

Arm title	somatoline

Arm description:

Levothyroxine 0,1% + escin 0,3%

Arm type	Experimental
Investigational medicinal product name	Somatoline (Levothyroxine 0,1% + escin 0,3%)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous emulsion
Routes of administration	Cutaneous use

Dosage and administration details:

2 sachets/day on the thighs for the first two days (10 g /die) , followed by one sachet (5 g for each thigh) up to 4 weeks

Number of subjects in period 1	somatoline
Started	24
Completed	20
Not completed	4
Lost to follow-up	4

Baseline characteristics

Reporting groups	
Reporting group title	all trial

Reporting group description:

A total of 24 adult women 33.4 (±6.1) years old (range 26-47) received at least one dose of SOMATOLINE and were all included in the ITT data set. All the patients adopted contraceptive methods. No comorbidities, concomitant treatments and abnormalities at the physical examination were reported at screening;
only, 2 patients suffered from minor ECG abnormalities: slight bundle branch block and left axial deviation.
6 patients were light smokers (mean 6.2 cigarettes per day, range 1-10) and only 8 occasionally drank alcohol; sports activities, always moderate, were practiced by 11 patients out of 24 (45.8%).
The patients declared a daily consumption of water outside meals of half liter or less in 25,0% (6/24) of cases, more than half liter, up to one liter, in 29,2% (7/24) and more than one liter in 45,8% (11/24) of the cases. All the patients but 3 (12.5%), referred a normal or moderate sodium intake.

Reporting group values	all trial	Total	
Number of subjects	24	24	
Age categorical			
A total of 24 adult women 33.4 (±6.1) years old (range 26-47) received at least one dose of SOMATOLINE and were all included in the ITT data set			
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)	24	24	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
all females			
Units: Subjects			
Female	24	24	
Male	0	0	

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The "Intention To Treat Set" (ITT) comprised all subjects who received at least one application of IMP, regardless of the treatment status

Subject analysis set title	Per Protocol set
Subject analysis set type	Per protocol

Subject analysis set description:

The "Per-Protocol Set" (PP) comprised all subjects in the ITT set, with the exclusion of subjects with major protocol deviations

Reporting group values	ITT	Per Protocol set	
Number of subjects	24	22	
Age categorical			
A total of 24 adult women 33.4 (±6.1) years old (range 26-47) received at least one dose of SOMATOLINE and were all included in the ITT data set			
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)	24	22	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
all females			
Units: Subjects			
Female	24	22	
Male	0	0	

End points

End points reporting groups

Reporting group title	somatoline
Reporting group description: Levothyroxine 0,1% + escin 0,3%	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: The "Intention To Treat Set" (ITT) comprised all subjects who received at least one application of IMP, regardless of the treatment status	
Subject analysis set title	Per Protocol set
Subject analysis set type	Per protocol
Subject analysis set description: The "Per-Protocol Set" (PP) comprised all subjects in the ITT set, with the exclusion of subjects with major protocol deviations	

Primary: Primary end-point

End point title	Primary end-point[1]
End point description: Proportion of patients with reduction of at least 2 points in the thigh CSS (Cellulite Severy Scale) score	
End point type	Primary
End point timeframe: 28 days	

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: No statistical analyses can be uploaded since it is one arm study.

End point values	somatoline	ITT	Per Protocol set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	24	22	
Units: number of patients	24	24	22	

Attachments (see zip file)	primary end-point - ITT and PP sets/PRIMARY ENDPOINT

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary end-points

End point title	Secondary end-points

End point description:

The secondary end-points listed in the study protocol were:
a) Evolution of CSS score measured on the thighs at 14 and 28 days of treatment.
b) Evolution of CSS subscores measured on the thighs at 14 and 28 days of treatment.
c) Evolution of PR-PCSS at 14 and 28 days of treatment.
d) Percentage of patients who achieved a composite ≥1-level improvement from baseline in CR-PCSS rating and PR-PCSS rating (secondary composite end point)
e) Evolution of thigh circumference measurements assessed at baseline, 14 and 28 days of

treatment
f) Changes in ultrasonographic structure of the cutaneous layers at 14 and 28 days of treatment
g) Change in subcutaneous microcirculation trough Laser Doppler Flowmetry
h) Patients' evaluation of the satisfaction.

End point type	Secondary
End point timeframe:	
14 and 28 days of treatment	

End point values	somatoline	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	24	24		
Units: number of patients	24	24		

Attachments (see zip file)	Secondary End-points ITT set/SECONDARY ENDPOINT

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From Informed Consent Signature to End of Study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Somatoline

Reporting group description:

all patients enrolled (single arm)

Serious adverse events	Somatoline		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (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 %

Non-serious adverse events	Somatoline		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No serious adverse events occurred; this was a study on young women with cellulite and study duration was 42 days per subject.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study limitations: There was no control arm, even if a chronic condition like cellulite mitigates the problem. This study involved a small sample size and a short treatment duration, typically a half, or less, of the recommended treatment duration.

Notes: