Clinical trial results:
A multicenter, placebo-controlled, single dose study in acute episodic and chronic cluster headache to evaluate the safety and efficacy of SOM230 subcutaneous (s.c.)

Summary

EudraCT number	2015-004436-34
Trial protocol	DE GB
Global end of trial date	25 September 2018

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	CSOM230Y2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02619617
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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	25 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 September 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess headache response of single s.c. dose of SOM230 compared to placebo in managing CH attack at 30 minutes post-dosing

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2016
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: 27
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Germany: 2
Worldwide total number of subjects	30
EEA total number of subjects	3

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)	29
From 65 to 84 years	1

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This non-confirmatory study was planned to be conducted in 2 Cohorts using a one-sequence two-period design to compare SOM230 vs. placebo. Two consecutive CH attacks were treated: the first attack was treated with placebo (Period 1) and the subsequent attack was treated with SOM230 (Period 2).
It was decided not to initiate Cohort 2.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Arm title	Placebo s.c. /1.5 mg SOM230 s.c.

Arm description:

A: single dose of placebo s.c. (Period 1) B: single dose of 1.5 mg s.c. SOM230 (Period 2)

Arm type	Experimental
Investigational medicinal product name	SOM230
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Cohort 1:
A: single dose of placebo s.c. (Cohort 1-Period 1)
B: single dose of 1.5 mg s.c. SOM230 (Cohort 1-Period 2)
Subjects received both treatments starting with placebo

Number of subjects in period 1	Placebo s.c. /1.5 mg SOM230 s.c.
Started	30
Completed	24
Not completed	6
Physician decision	5
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo s.c. /1.5 mg SOM230 s.c.
Reporting group description:	
A: single dose of placebo s.c. (Period 1) B: single dose of 1.5 mg s.c. SOM230 (Period 2)	

Reporting group values	Placebo s.c. /1.5 mg SOM230 s.c.	Total	
Number of subjects	30	30	
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)	28	28	
From 65-84 years	0	0	
85 years and over	0	0	
Not recorded	2	2	
Age Continuous			
Data for 2 patients were not recorded and thus not included in the mean age (SD) calculation. Subject demographics data on N=28 (the safety analysis set - included all subjects that received any study drug).			
Units: Years			
arithmetic mean	43.9		
standard deviation	± 10.55	-	
Sex: Female, Male Units: Subjects			
Female	6	6	
Male	22	22	
Not known	2	2	
Ethnicity (NIH/OMB)			
Data for 2 patients were not recorded and thus not included in the subject demographics data. Subject demographics data on N=28 (the safety analysis set - included all subjects that received any study drug).			
Units: Subjects			
Hispanic or Latino	3	3	
Not Hispanic or Latino	3	3	
Unknown or Not Reported	24	24	

End points

End points reporting groups

Reporting group title	Placebo s.c. /1.5 mg SOM230 s.c.
Reporting group description: A: single dose of placebo s.c. (Period 1) B: single dose of 1.5 mg s.c. SOM230 (Period 2)	
Subject analysis set title	SOM230 1.5 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description: single dose of 1.5 mg s.c. SOM230	
Subject analysis set title	Placebo s.c.
Subject analysis set type	Sub-group analysis
Subject analysis set description: A single dose of placebo s.c.	

Primary: Percent (%) of patients with headache response

End point title	Percent (%) of patients with headache response
End point description: Defined as very severe, severe, or moderate pain before dosing that becomes mild or nil at 30 minutes post-dosing	
End point type	Primary
End point timeframe: 30 minutes post dose	

End point values	SOM230 1.5 mg	Placebo s.c.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[1]	20[2]		
Units: Participants	10	9		

Notes:

[1] - these 20 patients in the SOM230 arm is the same 20 patients in the placebo arm.

[2] - these 20 patients in the SOM230 arm is the same 20 patients in the placebo arm.

Statistical analyses

Statistical analysis title	Percent of patients with headache response
Statistical analysis description: There are 20 patients total in this analysis (the 20 patients in the SOM230 arm are the same 20 patients in the placebo arm).	
Comparison groups	Placebo s.c. v SOM230 1.5 mg
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.698
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.308

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.419
upper limit	4.082

Notes:

[3] - 1.5mg SOM230 s.c. vs. Placebo s.c.

Secondary: Percent of patients who are pain free at 30 minutes post dose

End point title	Percent of patients who are pain free at 30 minutes post dose

End point description:

Percentage of subjects pain free and of subjects reporting improvement of associated autonomic symptoms (for example, lacrimation, blushing, pupil constriction, etc.) over time was tabulated by dose. Number and percentage of subjects who received rescue medication at or after 30 minutes.

End point type	Secondary

End point timeframe:

30 mins post dose

End point values	SOM230 1.5 mg	Placebo s.c.		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20[4]	20[5]		
Units: Participants	7	5		

Notes:

[4] - these 20 patients in the SOM230 arm is the same 20 patients in the placebo arm.

[5] - these 20 patients in the SOM230 arm is the same 20 patients in the placebo arm.

Statistical analyses

Statistical analysis title	Percent of patients pain-free 30-minutes post dose

Statistical analysis description:

There are 20 patients in this analysis (the 20 patients in the SOM230 arm are the same 20 patients in the placebo arm).

Comparison groups	Placebo s.c. v SOM230 1.5 mg
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.385
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.033
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.53
upper limit	7.79

Notes:

[6] - 1.5mg SOM230 s.c. vs. Placebo s.c.

Secondary: Hemoglobin

End point title	Hemoglobin

End point description:

Hematology lab parameters by treatment and time point

End point type	Secondary

End point timeframe:

throughout study, up up 9 days after treatment

End point values	Placebo s.c. /1.5 mg SOM230 s.c.			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: g/L				
arithmetic mean (standard deviation)				
Screening	153.4 (± 12.93)			
End of Study	149.5 (± 15.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pulse Rate

End point title	Pulse Rate

End point description:

Vital signs by treatment and time point

End point type	Secondary

End point timeframe:

throughout study, up up 9 days after treatment

End point values	Placebo s.c. /1.5 mg SOM230 s.c.			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Beats/min				
arithmetic mean (standard deviation)				
Screening	77.2 (± 15.02)			
Baseline	78.1 (± 11.99)			
Period 1	76.9 (± 12.77)			
Period 2	74.0 (± 10.86)			
End of Study	81.1 (± 13.50)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 26 months.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo s.c.
Reporting group description:	
Placebo s.c.	
Reporting group title	1.5 mg SOM230 s.c.
Reporting group description:	
1.5 mg SOM230 s.c.	

Serious adverse events	Placebo s.c.	1.5 mg SOM230 s.c.	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)	0 / 26 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Placebo s.c.	1.5 mg SOM230 s.c.	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 28 (17.86%)	23 / 26 (88.46%)	
Investigations			
Haematocrit decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Red blood cell count decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 28 (3.57%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 28 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 28 (3.57%)	6 / 26 (23.08%)	
occurrences (all)	1	6	
Injection site bruising			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Injection site erythema			
subjects affected / exposed	1 / 28 (3.57%)	4 / 26 (15.38%)	
occurrences (all)	1	4	
Injection site pain			
subjects affected / exposed	1 / 28 (3.57%)	5 / 26 (19.23%)	
occurrences (all)	1	5	
Injection site reaction			

subjects affected / exposed	1 / 28 (3.57%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Injection site warmth			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Vessel puncture site bruise			
subjects affected / exposed	1 / 28 (3.57%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 28 (0.00%)	3 / 26 (11.54%)	
occurrences (all)	0	3	
Flatulence			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	7 / 26 (26.92%)	
occurrences (all)	0	7	
Nausea			
subjects affected / exposed	0 / 28 (0.00%)	12 / 26 (46.15%)	
occurrences (all)	0	12	
Vomiting			
subjects affected / exposed	1 / 28 (3.57%)	7 / 26 (26.92%)	
occurrences (all)	1	7	
Respiratory, thoracic and mediastinal disorders			
Pleuritic pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Pruritus subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 26 (3.85%) 1	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	2 / 26 (7.69%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2016	Modified the study design to conduct Part A in 2 consecutive cohorts: assessment of the 1.5 mg dose of SOM230 (s.c.) versus placebo in the first Cohort; then, based on the 1.5 mg dose efficacy and safety data, the 0.9 mg dose may be evaluated in the second Cohort. Saliva biomarker assessment was removed from this study to minimize the burden on subjects given the nature of the study disease and the challenges in collecting these samples.
02 May 2016	Modified the study design to conduct a 2 period one- sequence design comparing SOM230 to Placebo. Study participants were expected to be mainly non-sumatriptan users (subjects who were non-tolerant, resistant or had contraindication for sumatriptan). Therefore enrolling subjects into Part B where a comparative sumatriptan arm was included was very difficult and Part B was eliminated. To increase statistical power a one-sequence two-period design with all subjects receiving placebo for the first attack and SOM230 for the second attack was used. Given the nature of the disease (repeated attacks up to 8 attacks/day for up to 2 months), the relatively long half-life of SOM230, and to ensure consistency between attacks, treating 2 consecutive attacks in a one-sequence two-period design with a fixed placebo treatment in Period 1 was more appropriate to CH subjects avoiding any carryover effects.
02 March 2017	Modified the study exclusion criteria required for male subjects' contraception and clarified some study descriptions.
02 March 2018	To allow for clinic domiciling of a subject if deemed appropriate by an Investigator. The UK site was executing the protocol amendment 2, while the US and Germany sites were executing the protocol amendment 3, as they reflect local Health Authority requirements for male contraception. Amendment 4 harmonized the protocol and accommodated differences in local Health Authority requirements for male contraception.

Notes:

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.

Terminated (Non-efficacy in first Phase 2a cohort.)

Notes: