Clinical trial results:
Clinical Trial to Evaluate the Efficacy and Safety of MACRORANGE® in Patients Suffering from Functional Constipation

Summary

EudraCT number	2018-001914-13
Trial protocol	BE
Global end of trial date	26 March 2019

Results information

Result version number	v1 (current)
This version publication date	15 May 2021
First version publication date	15 May 2021
Summary attachment (see zip file)	Summary (MACR001 CSR Synopsis 20190904_anonymous.pdf)

Trial information

Trial identification

Sponsor protocol code	MACR001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Salsarulo Pharma
Sponsor organisation address	8, rue de l'Est, Boulogne-Billancourt, France, 92100
Public contact	Gilles Salsarulo, Salsarulo Pharma, +33 618920881, gilles.salsarulo@salsapharma.com
Scientific contact	Gérard Salsarulo, Salsarulo Pharma, +33 148257764, gerard.salsarulo@wanadoo.fr

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	30 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2019
Global end of trial reached?	Yes
Global end of trial date	26 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of MACRORANGE® in patients with functional constipation (according to Rome III criteria) after daily administration of MACRORANGE® up to 14 days.

Protection of trial subjects:

The study was conducted in accordance with International Conference on Harmonisation, Good Clinical Practice (ICH-GCP E6R2), the ethical principles that have their origins in the Declaration of Helsinki (revised Edinburgh, 2000), and applicable national and local regulatory requirements.

Prior to the performance of any study-specific procedures, written informed consent was obtained from each patient. The patient was informed about the nature and purpose of the study, as well as of its risks and benefits.
It was explained that the patient could withdraw from the study at any time for any reason and that this would not have any effect on potential future medical care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 November 2018
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	Belgium: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at a single site at Advanced Technology Corporation (ATC) Pharma S.A., Liège, Belgium. The first patient was screened and signed informed consent document on 05 November 2018 (first patient / first visit).

Pre-assignment

Screening details:

Patients attended the site to enter the screening period within 21 days prior to dosing (Day 1). 40 patients were screened to get 30 patients enrolled. The main reasons for screen failure consisted either in the inclusion/exclusion criteria that were not fulfilled (e.g. Irritable Bowel Syndrome) or a consent withdrawal for personal reasons.

Period 1

Period 1 title	Wash-out
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	wash-out

Arm description:

wash-out

Arm type	wash-out
Investigational medicinal product name	none
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral paste in sachet
Routes of administration	Oral use

Dosage and administration details:

no product - wash-out period

Number of subjects in period 1	wash-out
Started	30
Completed	30

Period 2

Period 2 title	Macrorange
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Macrorange

Arm description:

MACRORANGE® was administered as 12 g single dose stick-pack, corresponding to a dosage of 5.04 g of Macrogol 4000. The dose regimen started with a fixed dose of MACRORANGE® for 2 days, with 3 stick packs on Day 1 and 2 stick-packs on Day 2, and then was flexible from Day 3 to Day 14 (with 1 to 2 stick-pack per day), as decided by the patient and based on the number of defecations per day. The patient was instructed to take one single dose stick-pack of MACRORANGE® per day if he/she defecated at least once during that day, or two single dose stick-packs of MACRORANGE® per day if he/she did not defecate at all during that day.

Arm type	Experimental
Investigational medicinal product name	Macrorange
Investigational medicinal product code	MACROGOL 4000
Other name	
Pharmaceutical forms	Oral paste in sachet
Routes of administration	Oral use

Dosage and administration details:

MACRORANGE® was administered as 12 g single dose stick-pack, corresponding to a dosage of 5.04 g of Macrogol 4000. The dose regimen started with a fixed dose of MACRORANGE® for 2 days, with 3 stick packs on Day 1 and 2 stick-packs on Day 2, and then was flexible from Day 3 to Day 14 (with 1 to 2 stick-pack per day), as decided by the patient and based on the number of defecations per day. The patient was instructed to take one single dose stick-pack of MACRORANGE® per day if he/she defecated at least once during that day, or two single dose stick-packs of MACRORANGE® per day if he/she did not defecate at all during that day.

Number of subjects in period 2	Macrorange
Started	30
Completed	30

Baseline characteristics

Reporting groups	
Reporting group title	Wash-out

Reporting group description: -

Reporting group values	Wash-out	Total	
Number of subjects	30	30	
Age categorical Units: Subjects			
Adults (18-64 years)	30	30	
Age continuous Units: years median full range (min-max)	 37 23 to 63	 -	
Gender categorical Units: Subjects			
Female	21	21	
Male	9	9	

End points

End points reporting groups

Reporting group title	wash-out
Reporting group description: wash-out	
Reporting group title	Macrorange
Reporting group description: MACRORANGE® was administered as 12 g single dose stick-pack, corresponding to a dosage of 5.04 g of Macrogol 4000. The dose regimen started with a fixed dose of MACRORANGE® for 2 days, with 3 stick packs on Day 1 and 2 stick-packs on Day 2, and then was flexible from Day 3 to Day 14 (with 1 to 2 stick-pack per day), as decided by the patient and based on the number of defecations per day. The patient was instructed to take one single dose stick-pack of MACRORANGE® per day if he/she defecated at least once during that day, or two single dose stick-packs of MACRORANGE® per day if he/she did not defecate at all during that day.	

Primary: Average number of complete spontaneous defecations for the treatment period

End point title	Average number of complete spontaneous defecations for the treatment period
End point description:	
End point type	Primary
End point timeframe: The average number of complete spontaneous defecations for the 2-week treatment with MACRORANGE®	

End point values	Macrorange	wash-out		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: number per week				
arithmetic mean (standard deviation)	5.44 (± 2.08)	2.95 (± 1.90)		

Statistical analyses

Statistical analysis title	Change from Baseline in Defecations
Comparison groups	Macrorange v wash-out
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 2-sided

Secondary: Average number of complete spontaneous defecations (Week 1)

End point title	Average number of complete spontaneous defecations (Week 1)

End point description:

End point type	Secondary

End point timeframe:

The average number of complete spontaneous defecations during the treatment periods from Day 1 (post-dose) to Day 8 (pre-dose)

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number per week				
arithmetic mean (standard error)	5.43 (± 2.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average number of complete spontaneous defecations (Week 2)

End point title	Average number of complete spontaneous defecations (Week 2)

End point description:

End point type	Secondary

End point timeframe:

The average number of complete spontaneous defecations during the treatment periods from from Day 8 (post-dose) to Day 14.

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number per week				
arithmetic mean (standard error)	5.44 (± 2.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average of daily dosage of MACRORANGE (Week 1)

End point title	Average of daily dosage of MACRORANGE (Week 1)

End point description:

End point type	Secondary

End point timeframe:

The average daily dosage of MACRORANGE® as grams of macrogol 4000 from Day 1 to Day 8 pre-dose (Week 1)

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: grams of macrogol 4000				
arithmetic mean (standard error)	8.54 (± 0.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average of daily dosage of MACRORANGE (Week 2)

End point title	Average of daily dosage of MACRORANGE (Week 2)

End point description:

End point type	Secondary

End point timeframe:

The average daily dosage of MACRORANGE® as grams of macrogol 4000 from Day 8 (post-dose) to Day 14 (Week 2)

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: grams of macrogol 4000				
arithmetic mean (standard error)	6.89 (± 1.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Efficacy (Patient’s evaluation)

End point title	Global Efficacy (Patient’s evaluation)

End point description:

End point type	Secondary

End point timeframe:

Global efficacy of MACRORANGE® was assessed by the patient at the end of the 2-week treatment period.

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number				
Poor	6			
Moderate	5			
Good	15			
Very Good	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Taste of MACRORANGE

End point title	Taste of MACRORANGE

End point description:

End point type	Secondary

End point timeframe:

Taste of MACRORANGE® was assessed by the patient at the end of the 2-week treatment period.

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number				
Dislike very much	0			
Dislike slightly	1			
Like slightly	20			
Like very much	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Efficacy (Independent rater's evaluation)

End point title	Global Efficacy (Independent rater's evaluation)

End point description:

End point type	Secondary

End point timeframe:

Global efficacy of MACRORANGE® were assessed by independent reader at the end of the 2-week treatment period.

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number				
Poor	4			
Moderate	8			
Good	12			
Very Good	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Global Tolerance (Independent rater’s evaluation)

End point title	Global Tolerance (Independent rater’s evaluation)

End point description:

End point type	Secondary

End point timeframe:

Global Tolerance of MACRORANGE® were assessed by independent reader at the end of the 2-week treatment period.

End point values	Macrorange			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number				
Poor	0			
Moderate	4			
Good	15			
Ver Good	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Stool Consistency

End point title	Stool Consistency

End point description:

Stool consistency as assessed by the patient by using the Bristol scale

End point type	Secondary

End point timeframe:

during wash-out period and from Day 8, post-dose to Day 14

End point values	Macrorange	wash-out		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30[1]	30[2]		
Units: number				
Separate hard lumps, like nuts	3	17		
Sausage-shaped but lumpy	9	26		
Like a sausage but with cracks on its surface	29	29		
Like a sausage or snake, smooth and soft	74	15		
Soft blobs with clear-cut edges (passed easily)	17	4		
: Fluffy pieces with ragged edges, a mushy stool	8	9		
Watery, no solid pieces, entirely liquid	0	1		

Notes:

[1] - n=140 stools

[2] - n=101 stools

Statistical analyses

Statistical analysis title	Chi-test

Statistical analysis description:

chi-squared test

Comparison groups	Macrorange v wash-out
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

Other pre-specified: Average number of complete spontaneous defecations (at baseline)

End point title	Average number of complete spontaneous defecations (at baseline)

End point description:

End point type	Other pre-specified

End point timeframe:

Average number of complete spontaneous defecations at the end of baseline period (7 days wash-out)

End point values	wash-out			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: number per week				
arithmetic mean (standard deviation)	2.95 (± 1.90)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Collection of adverse event was performed from screening to end of trial, during on-site visits.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21

Reporting groups	
Reporting group title	Safety population
Reporting group description: all subjects who received at least one dose of IMP	

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (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	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 30 (43.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	4		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	9 / 30 (30.00%)		
occurrences (all)	15		
Abdominal pain			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Vomiting			

subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Furuncle			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

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.

Open label study - no comparator

Notes: