Clinical trial results:
Efficacy and Tolerability of Menthacarin in Patients (>= 18 years old) suffering from symptoms of Irritable Bowel Syndrome (IBS)

Summary

EudraCT number	2014-004702-14
Trial protocol	DE
Global end of trial date	15 June 2018

Results information

Result version number	v1 (current)
This version publication date	14 June 2020
First version publication date	14 June 2020
Summary attachment (see zip file)	530079.01.302 Summary of results 2020_05_29 (750598.01.003 SummaryOfResults_EUDRA_CT_Version 1.0_ 20191220 Final_mit Schwärzung.pdf)

Trial information

Trial identification

Sponsor protocol code	530079.01.302

Additional study identifiers

ISRCTN number	ISRCTN31630783
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr. Willmar-Schwabe GmbH & Co. KG
Sponsor organisation address	Willmar-Schwabe-Str. 4, Karlsruhe, Germany, 76227
Public contact	Head of Clinical Research Department, Dr. Willmar Schwabe GmbH & Co. KG, 49 7214005573,
Scientific contact	Head of Clinical Research Department, Dr. Willmar Schwabe GmbH & Co. KG, 49 7214005573,

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	16 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 June 2018
Global end of trial reached?	Yes
Global end of trial date	15 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and tolerability of Menthacarin® in patients (>= 18 years old) suffering from symptoms of IBS.

Protection of trial subjects:

Possibility to withdraw informed consent. Monitoring of adverse events and laboratory parameters.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 July 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	Germany: 226
Worldwide total number of subjects	226
EEA total number of subjects	226

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)	205
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Twenty-two trial centres in Germany participated in the trial.

Pre-assignment

Screening details:

A total of 226 patients were screened for enrollment into the trial. Four patients were re-screened and received a new patient number. Therefore, 230 patient numbers exist. Twenty-six of the 226 screened patients were not randomized and did not receive trial medication. One patient was randomized but did not take study medication.

Pre-assignment period milestones

Number of subjects started	226
Number of subjects completed	199

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening Failures: 20
Reason: Number of subjects	Consent withdrawn by subject: 5
Reason: Number of subjects	Scheduling Issues: 2

Period 1

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

Blinding implementation details:

Double blind

Arms

Are arms mutually exclusive?	Yes
Arm title	Menthacarin

Arm description:

Menthacarin (Mentha x piperita L. (90 mg WS® 1340) and Carum carvi (50 mg WS® 1520)), 1 soft capsule taken 2 times daily (1-1-0)

Arm type	Experimental
Investigational medicinal product name	WS® 1340 / WS® 1520
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

1-1-0

Arm title	Placebo

Arm description:

Placebo, 1 soft capsule taken 2 times daily (1-1-0)

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

1-1-0

Number of subjects in period 1[1]	Menthacarin	Placebo
Started	100	99
Completed	93	94
Not completed	7	5
Consent withdrawn by subject	2	1
Adverse event, non-fatal	3	1
Other reason	-	1
Lost to follow-up	1	-
Lack of efficacy	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: In total, 27 of the 226 subjects screened for inclusion into the study were not included into the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Menthacarin
Reporting group description:	
Menthacarin (Mentha x piperita L. (90 mg WS® 1340) and Carum carvi (50 mg WS® 1520)), 1 soft capsule taken 2 times daily (1-1-0)	
Reporting group title	Placebo
Reporting group description:	
Placebo, 1 soft capsule taken 2 times daily (1-1-0)	

Reporting group values	Menthacarin	Placebo	Total
Number of subjects	100	99	199
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	89	91	180
From 65-84 years	11	8	19
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	41.9	39.7	
standard deviation	± 15.8	± 14.3	-
Gender categorical			
Units: Subjects			
Female	80	76	156
Male	20	23	43

Subject analysis sets	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS included all patients of the Safety analysis set who had at least one measure of the primary efficacy parameter (pain score for 7 days to allow the calculation of a weekly average) during the active treatment period after baseline visit and patients who terminated the trial prematurely because of lack of efficacy or unexpected improvement/remission of disease (after at least 14 days of treatment) or an AE for which a causal relationship to trial medication was not excluded (even if the patient had no efficacy measurement during active treatment period).	

Reporting group values	Full Analysis Set		
Number of subjects	196		

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)	177		
From 65-84 years	19		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	41.0		
standard deviation	± 15.1		
Gender categorical Units: Subjects			
Female	153		
Male	43		

End points

End points reporting groups

Reporting group title	Menthacarin

Reporting group description:

Menthacarin (Mentha x piperita L. (90 mg WS® 1340) and Carum carvi (50 mg WS® 1520)), 1 soft capsule taken 2 times daily (1-1-0)

Reporting group title	Placebo

Reporting group description:

Placebo, 1 soft capsule taken 2 times daily (1-1-0)

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS included all patients of the Safety analysis set who had at least one measure of the primary efficacy parameter (pain score for 7 days to allow the calculation of a weekly average) during the active treatment period after baseline visit and patients who terminated the trial prematurely because of lack of efficacy or unexpected improvement/remission of disease (after at least 14 days of treatment) or an AE for which a causal relationship to trial medication was not excluded (even if the patient had no efficacy measurement during active treatment period).

Primary: Change in abdominal pain (using an 11 point numeric rating scale (NRS))

End point title	Change in abdominal pain (using an 11 point numeric rating scale (NRS))[1]

End point description:

Note: This document in its section "End points" specifies commercially confidential information of Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe referred to in Article 81 Section (4) b) Regulation (EU) 536/2014 that is a trade secret and released by the holder for purposes of Regulation (EU) 536/2014 only under the conditon of confidence. Trade secrets may not - even in part - be published or released to third parties other than to competent authorities without express permission of the trade secret holder.

End point type	Primary

End point timeframe:

Day 0 and Day 28

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: The reported results are chosen freely. See document for a complete description of the statistical methods and results.
Statistical analyses were conducted for the end point. Refer to the attached summary of results for details.

End point values	Menthacarin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	99		
Units: points				
median (confidence interval 95%)	9999.99 (9999.99 to 9999.99)	9999.99 (9999.99 to 9999.99)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12 weeks	
Adverse event reporting additional description:	
Efficacy and tolerability of Carmenhtin in patients suffering from irritable bowel syndrome	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	No active treatment
Reporting group description:	
No active treatment	
Reporting group title	Menthacarin
Reporting group description:	
Study medication	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	No active treatment	Menthacarin	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	1 / 139 (0.72%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	0 / 200 (0.00%)	0 / 194 (0.00%)	1 / 139 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	0 / 200 (0.00%)	1 / 194 (0.52%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	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	No active treatment	Menthacarin	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 200 (1.50%)	8 / 194 (4.12%)	9 / 139 (6.47%)
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 200 (1.50%)	8 / 194 (4.12%)	9 / 139 (6.47%)
occurrences (all)	3	8	9

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