Clinical trial results:
Double-blind, randomized, placebo-controlled clinical trial to evaluate the safety and efficacy of „Ensinger Schiller Quelle Heilwasser“ on improvement of bowel function

Summary

EudraCT number	2013-000861-36
Trial protocol	DE
Global end of trial date	26 May 2014

Results information

Result version number	v1 (current)
This version publication date	15 January 2022
First version publication date	15 January 2022
Summary attachment (see zip file)	Synopsis_incl_results_ENS007612 (2015_08_06_Synopsis_ENS007612.pdf)

Trial information

Trial identification

Sponsor protocol code	ENS/007612

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Ensinger Mineral-Heilquellen GmbH
Sponsor organisation address	Horrheimer Straße 28-36, Vaihingen-Ensingen, Germany,
Public contact	Thomas Fritz, Ensinger Mineral-Heilquellen GmbH, 0049 70422809610, thomas.fritz@ensinger.de
Scientific contact	Thomas Fritz, Ensinger Mineral-Heilquellen GmbH, 0049 70422809610, thomas.fritz@ensinger.de

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	06 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 May 2014
Global end of trial reached?	Yes
Global end of trial date	26 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is the change of bowel movement frequency per week between baseline and visit 4 compared to placebo.

Protection of trial subjects:

As no pain and distress was expected no specific measures were taken.

Background therapy:

No other treatments was used across all arms/groups in the trial .

Evidence for comparator:

In order to obtain objective study data and to better assess the effect of the healing water, a placebo was used as a comparator, a product with an identical appearance and similar taste, but with a low concentration of minerals and a CO2 concentration comparable to the verum.

Actual start date of recruitment	30 July 2013
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: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	100

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment take place in Germany at one site in the period from 30. July 2013 until 26. May 2014.

Pre-assignment

Screening details:

Detailed information provided to the patient by the investigator about the content, benefits and risks of this clinical trial.
- written consent of the patient to participate
Bowel movements on 2 - 4 days per week during the last 3 months
- Functional constipation according to ROM III criteria

Period 1

Period 1 title	visit 2 - 4 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Verum

Arm description:

50% of all recruited subjects took the investigational drug during the study.

Arm type	Experimental
Investigational medicinal product name	Ensinger Schiller Quelle Heilwasser
Investigational medicinal product code	58415.00.00
Other name	
Pharmaceutical forms	Oral solution in bottle
Routes of administration	Oral use

Dosage and administration details:

Dosage: 250 ml fasting in the morning / 250 ml in the course of the morning / 250 ml approx. 30 min before lunch / 250 ml approx. 30 min before dinner

Arm title	Placebo

Arm description:

50% of all recruited subjects took the placebo during the study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Daily intake of a total of 1 litre (room temperature):
- 250 ml on an empty stomach in the morning
- 250 ml in the course of the morning
- 250 ml approx. 30 min before lunch
- 250 ml approx. 30 min before dinner

Number of subjects in period 1	Verum	Placebo
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups

Reporting group title	visit 2 - 4

Reporting group description: -

Reporting group values	visit 2 - 4	Total	
Number of subjects	100	100	
Age categorical			
Subjects included has been between 18 and 64 years old.			
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)	100	100	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	44.8		
standard deviation	± 11.4	-	
Gender categorical			
Units: Subjects			
Female	85	85	
Male	15	15	

Subject analysis sets

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

Subject analysis set description:

The FAS (full analyses set) population includes all subjects with no major violations (as judged during the data review) of inclusion and exclusion criteria at the timepoint of the enrollment, who have taken the investigational product at least one time and subjects whose benefit parameters are available.

Subject analysis set title	Valid Case Analysis Set
Subject analysis set type	Per protocol

Subject analysis set description:

The VCAS (valid case analyses set) population is composed of all subjects in the FAS popula- tion with no major protocol violations (to be documented during data review).

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety set: All subjects who had consumed the investigational product (IP) at least once (as per diary records) will be included in the safety set.

Reporting group values	Full Analysis Set	Valid Case Analysis Set	Safety
Number of subjects	100	69	100
Age categorical			
Subjects included has been between 18 and 64 years old.			
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)	100	69	100
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	44.8	42.7	44.8
standard deviation	± 11.4	± 11.7	± 11.4
Gender categorical			
Units: Subjects			
Female	85	58	85
Male	15	11	15

End points

End points reporting groups

Reporting group title	Verum
Reporting group description:	
50% of all recruited subjects took the investigational drug during the study.	
Reporting group title	Placebo
Reporting group description:	
50% of all recruited subjects took the placebo during the study.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS (full analyses set) population includes all subjects with no major violations (as judged during the data review) of inclusion and exclusion criteria at the timepoint of the enrollment, who have taken the investigational product at least one time and subjects whose benefit parameters are available.	
Subject analysis set title	Valid Case Analysis Set
Subject analysis set type	Per protocol
Subject analysis set description:	
The VCAS (valid case analyses set) population is composed of all subjects in the FAS popula- tion with no major protocol violations (to be documented during data review).	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety set: All subjects who had consumed the investigational product (IP) at least once (as per diary records) will be included in the safety set.	

Primary: Change of stool frequency

End point title	Change of stool frequency
End point description:	
Change in stool frequency per week between baseline and visit 4 compared to placebo. For this purpose, the stool frequency in the week before the baseline visit is compared with the stool frequency in the week before visit 4 (using the patient diary).	
End point type	Primary
End point timeframe:	
Between Baseline and visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: Numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Numbers	100			

Statistical analyses

Statistical analysis title	Wilcoxon
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change of stool frequency per week

End point title	Change of stool frequency per week

End point description:

Change in stool frequency per week between baseline and visit 3 compared to placebo. The stool frequency in the week before the baseline visit is compared with the stool frequency in the week before visit 3.

End point type	Secondary

End point timeframe:

Between baseline and visit 3

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: numbers	100			

Statistical analyses

Statistical analysis title	Exploratory
Statistical analysis description:	
All primary and secondary endpoints , as well as safety variables and other study-relevant parameters, were explored and analyzed descriptively.	
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Changes stoolfrequency during study duration	
End point title	Changes stoolfrequency during study duration
End point description:	
Change in stool frequency throughout the course of the study.	
End point type	Secondary
End point timeframe:	
During study duration	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: numbers	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Placebo v Verum

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided

Secondary: Changes in stool consistency

End point title	Changes in stool consistency

End point description:

Change in stool consistency between baseline and visit 3 and baseline and visit 4 compared to placebo.
Placebo (using Bristol Stool Form Scale questionnaire)

End point type	Secondary

End point timeframe:

Between baseline and visit 3
Between baseline and visit 4

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: number of kind of consistency	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: number of kind of consistency	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Placebo v Verum
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)

Confidence interval	
sides	2-sided

Secondary: Change in gastrointestinal well-being

End point title	Change in gastrointestinal well-being

End point description:

Change in gastrointestinal well-being
between baseline and visit 3 and baseline and visit 4 compared to placebo using the Gastrointestinal Quality of Life Index (GLQI).

End point type	Secondary

End point timeframe:

between baseline and visit 3 and baseline and visit 4

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: Score	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Score	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change in general well-being

End point title	Change in general well-being
End point description:	
Change in general well-being between baseline and visit 3 and baseline and visit 4 compared to placebo using SF-12 questionnaire.	
End point type	Secondary
End point timeframe:	
between baseline and visit 3 and baseline and visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: Score	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Score	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change in liver function parameters	
End point title	Change in liver function parameters
End point description:	
Change in liver function parameters between screening visit 1 and visit 4 compared to placebo.	
End point type	Secondary
End point timeframe:	
between screening visit 1 and visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: Decimal numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Decimal numbers	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change in lipid metabolism parameter

End point title	Change in lipid metabolism parameter
End point description:	
Change in lipid metabolism parameter between screening visit and visit 4 compared to placebo	
End point type	Secondary
End point timeframe:	
between screening visit and visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: Decimal numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Decimal numbers	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change in intestinal flora parameters

End point title	Change in intestinal flora parameters
End point description: Change in intestinal flora parameters between screening visit and visit 4 compared to placebo.	
End point type	Secondary
End point timeframe: between screening visit and visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: decimal numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: decimal numbers	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change in body weight

End point title	Change in body weight
End point description:	
Change in body weight between baseline and visit 3 as well as baseline and visit 4 compared with placebo	
End point type	Secondary
End point timeframe:	
between baseline and visit 3 as well as baseline and visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: Kilo gramm	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Kilo gramm	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change in abdominal and hip circumference

End point title	Change in abdominal and hip circumference

End point description:

Change in abdominal and hip circumference between baseline and visit 3 and baseline and visit 4 compared to placebo.

End point type	Secondary

End point timeframe:

between baseline and visit 3 and baseline and visit 4

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: cm	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: cm	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Change in blood pressure

End point title	Change in blood pressure

End point description:

Change in blood pressure between baseline and visit 3 and baseline and visit 4 compared to placebo.

End point type	Secondary

End point timeframe:

between baseline and visit 3 and baseline and visit 4

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: mm/Hg				
number (not applicable)	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: mm/Hg				
number (not applicable)	100			

Statistical analyses

Statistical analysis title	Exploratory
Comparison groups	Verum v Placebo

Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Confidence interval	
sides	2-sided
Variability estimate	Standard deviation

Secondary: Global assessment of effectiveness

End point title	Global assessment of effectiveness
End point description:	
Global assessment of effectiveness by investigators and Patients on visit 4	
End point type	Secondary
End point timeframe:	
on visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: numbers	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Global assessment of tolerability

End point title	Global assessment of tolerability
End point description:	
Global assessment of tolerability by investigators and patients on visit 4	
End point type	Secondary
End point timeframe:	
on visit 4	

End point values	Verum	Placebo	Full Analysis Set	Valid Case Analysis Set
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	50	50	100	69
Units: Numbers	50	50	100	69

End point values	Safety			
Subject group type	Subject analysis set			
Number of subjects analysed	100			
Units: Numbers	100			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From visit 2 until visit 4

Adverse event reporting additional description:

An adverse event (AE) is any adverse occurrence that happens to an affected person who has been administered an investigational medicinal product and that is not necessarily causally related to this treatment (GCP-V §3 No. 6).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	diarrhoe
Reporting group description: -	
Reporting group title	meteorismus

Reporting group description: -

Serious adverse events	diarrhoe	meteorismus	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (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	diarrhoe	meteorismus	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
occurrences (all)	1	1	
meteorism			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
occurrences (all)	1	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

None reported