Clinical trial results:
Opium tincture against chronic diarrhea - Healthy:
An investigator initiated, randomized placebo-controlled, double-blinded, cross-over, clinical trial

Summary

EudraCT number	2020-004875-41
Trial protocol	DK
Global end of trial date	05 June 2022

Results information

Result version number	v1 (current)
This version publication date	28 October 2022
First version publication date	28 October 2022

Trial information

Trial identification

Sponsor protocol code	Dropizol_healthy_2020

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Mech-Sense, Aalborg University Hospital
Sponsor organisation address	Mølleparkvej 4, Aalborg, Denmark, 9000
Public contact	Tina Okdahl , Mech-Sense, Aalborg University Hospital, +45 97663520, t.okdahl@rn.dk
Scientific contact	Tina Okdahl , Mech-Sense, Aalborg University Hospital, 97663520 97663520, t.okdahl@rn.dk

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	11 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2022
Global end of trial reached?	Yes
Global end of trial date	05 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective of the trial is to describe the efficacy and safety of opium tincture (Dropizol (R), Pharmanovia A/S, Denmark) against chronic diarrhea

Protection of trial subjects:

Subjects were instructed to report all experienced side effects in a diary, which was monitored throughout the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2020
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	Denmark: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	18
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was initiated in 2020 and was finalized in 2022

Pre-assignment

Screening details:

A medical doctor screened al subjects according to the inclusion and exclusion criteria

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Active treatment

Arm description:

Subjects receiving active treatment (opium tincture)

Arm type	Active comparator
Investigational medicinal product name	Opium Tincture
Investigational medicinal product code	
Other name	Dropizol
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

3x5 drops on day 1, 3x10 drops on day 2-9

Arm title	Placebo

Arm description:

Subjects receiving placebo

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

Dosage and administration details:

3*5 drops on day 1, 3x10 drops on day 2-9

Number of subjects in period 1	Active treatment	Placebo
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups

Reporting group title	Intervention

Reporting group description: -

Reporting group values	Intervention	Total	
Number of subjects	20	20	
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)	18	18	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
median	24		
inter-quartile range (Q1-Q3)	22 to 26	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	10	10	

End points

End points reporting groups

Reporting group title	Active treatment
Reporting group description:	
Subjects receiving active treatment (opium tincture)	
Reporting group title	Placebo
Reporting group description:	
Subjects receiving placebo	

Primary: Change in colonic transit time

End point title	Change in colonic transit time
End point description:	
End point type	Primary
End point timeframe:	
Change in transit time between during active and placebo treatment	

End point values	Active treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Hours				
median (inter-quartile range (Q1-Q3))	49 (40 to 73)	23 (16 to 38)		

Statistical analyses

Statistical analysis title	Colonc transit - mixed model
Statistical analysis description:	
Data were compared using a repeated measures mixed model with treatment (placebo, opium tincture) and segments (stomach, small bowel, colon, and whole gut) and as factors. In cases of significant findings, a subsequent Bonferroni-corrected post hoc analysis accounting for multiple comparisons was performed to investigate which segments differed between treatments.	
Comparison groups	Placebo v Active treatment
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Confidence interval	
level	95 %
sides	2-sided

Secondary: Daily bowel movements

End point title	Daily bowel movements

End point description:

End point type	Secondary

End point timeframe:

Subjects reported daily bowel movements during the entire study period

End point values	Active treatment	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Daily bowel movements				
arithmetic mean (standard deviation)	0.7 (± 0.4)	1.2 (± 0.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were collected from the time of inclusion to 5 days after study end	
Adverse event reporting additional description:	
Adverse events were noted by subjects in a diary, and study personel also asked about adverse events at vistis and follow-up calls	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Reporting groups	
Reporting group title	During intervention
Reporting group description: -	
Reporting group title	During placebo
Reporting group description: -	

Serious adverse events	During intervention	During placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (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: 5 %

Non-serious adverse events	During intervention	During placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 20 (75.00%)	8 / 20 (40.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 20 (45.00%)	4 / 20 (20.00%)	
occurrences (all)	9	4	
Fatigue			
subjects affected / exposed	8 / 20 (40.00%)	2 / 20 (10.00%)	
occurrences (all)	8	2	
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	7 / 20 (35.00%) 7	0 / 20 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 4	2 / 20 (10.00%) 2	

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