



## 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 all 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               |
| <b>Arm title</b>             | 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

|                  |         |
|------------------|---------|
| <b>Arm title</b> | 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

| <b>Number of subjects in period 1</b> | 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                                                                                                                                                                                                                                                                                                                                                     | Colonic 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 ( $\pm$ 0.4) | 1.2 ( $\pm$ 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 personnel also asked about adverse events at visits 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 | 7 / 20 (35.00%) | 0 / 20 (0.00%)  |  |
| occurrences (all)           | 7               | 0               |  |
| Constipation                |                 |                 |  |
| subjects affected / exposed | 4 / 20 (20.00%) | 2 / 20 (10.00%) |  |
| occurrences (all)           | 4               | 2               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported