



## Clinical trial results:

### The effect of early administered cineole on the course of a common cold

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-000860-51 |
| Trial protocol           | DE             |
| Global end of trial date | 19 May 2021    |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 30 November 2022 |
| First version publication date | 30 November 2022 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | CASK0120 |
|-----------------------|----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Cassella-med GmbH & Co. KG  |
| Sponsor organisation address | Gereonsmühlengasse 1, Cologne, Germany, 50670   |
| Public contact               | Global Scientific Development & Clinical Operations, Cassella-med GmbH & Co. KG, +49 2211652565, clinical.operations@klosterfrau.de |
| Scientific contact           | Global Scientific Development & Clinical Operations, Cassella-med GmbH & Co. KG, +49 2211652565, clinical.operations@klosterfrau.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                       | 07 July 2021 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 19 May 2021  |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 19 May 2021  |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The objective of this clinical trial is to investigate the relation between timing of treatment onset with cineole and course of a common cold with or without acute bronchitis.

Protection of trial subjects:

A SARS-CoV-2 test was performed at visit 2 to exclude Covid-19 positive patients from participation at the study.

Despite this, in the event of fever and / or profound / protracted pain the patients were allowed to use rescue medication (paracetamol 500 mg).

Background therapy:

Not applicable.

Evidence for comparator:

As this trial aimed to investigate the relation between the timing of treatment onset with cineole and the course of a common cold with or without acute bronchitis, there was no treatment concurrent control or active comparator concurrent control.

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 17 September 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 | Germany: 522 |
| Worldwide total number of subjects   | 522          |
| EEA total number of subjects         | 522          |

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)                      | 505 |

|                     |    |
|---------------------|----|
| From 65 to 84 years | 17 |
| 85 years and over   | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The subjects were recruited in 25 practices of general practitioners, otolaryngologists and specialists in internal medicine throughout Germany from 17th September 2020 until 19th May 2021.

### Pre-assignment

Screening details:

Adult outpatients recollecting having at least 1 common cold in the last winter season were eligible for study participation if they meet all of the inclusion and exclusion criteria.

### Period 1

|                              |                 |
|------------------------------|-----------------|
| Period 1 title               | Screening phase |
| Is this the baseline period? | No              |
| Allocation method            | Not applicable  |
| Blinding used                | Not blinded     |

### Arms

|   |                 |
|---|-----------------|
| Arm title   | Screening Phase |
| Arm description: -  |                 |
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

|                                       |                 |
|---------------------------------------|-----------------|
| <b>Number of subjects in period 1</b> | Screening Phase |
| Started                               | 522             |
| Completed                             | 522             |

### Period 2

|                              |                |
|------------------------------|----------------|
| Period 2 title               | Illness phase  |
| Is this the baseline period? | No             |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

### Arms

|   |                   |
|---|-------------------|
| <b>Arm title</b>  | Onset of symptoms |
| Arm description: -  |                   |
| Arm type  | No intervention   |
| No investigational medicinal product assigned in this arm |                   |

|   |                   |
|---|-------------------|
| <b>Number of subjects in period 2<sup>[1]</sup></b> | Onset of symptoms |
| Started   | 329               |
| Completed   | 329               |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all patients fulfilled the criteria to enter the next period.

### Period 3

|                              |                    |
|------------------------------|--------------------|
| Period 3 title               | Treatment phase    |
| Is this the baseline period? | Yes <sup>[2]</sup> |
| Allocation method            | Not applicable     |
| Blinding used                | Not blinded        |

### Arms

|                              |       |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | ≤12 h |

Arm description:

Time to treatment stratum ≤12 h

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Soledum® forte capsules                      |
| Investigational medicinal product code | R05CA13                                      |
| Other name                             | German original name: Soledum® Kapseln forte |
| Pharmaceutical forms                   | Gastro-resistant capsule, soft               |
| Routes of administration               | Oral use                                     |

Dosage and administration details:

The IMP will be administered at home three times a day (morning, noon, evening, t.i.d.: 3x1 capsules). Treatment starts on the day of Visit 2 (Day 1) at the trial site and ends on the day of Visit 4 (Day 15±2) at home. Subjects, who recover from common cold before Visit 4, may terminate the administration of the IMP, once the first 10 WURSS-11 questions were rated by the subject "0" on two consecutive assessments in the eDiary.

On Day 1 (start of treatment), the IMP will be administered once (1x1 capsule), twice (2x1 capsule) or three times (3x1 capsule) by the subject depending on the time of Visit 2. On the day of Visit 4 (Day 15±2), the IMP will only be administered once in the morning (1x1 capsule, last dose).

IMP has to be swallowed unchewed with sufficient fluid (preferably one glass of water [200 mL]), but no hot beverage, approximately half an hour before a meal. Subjects with a sensitive stomach are recommended to take the IMP during their regular meals.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | >12 to 24 h |
|------------------|-------------|

Arm description:

Time to treatment stratum >12 to 24 h

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Soledum® forte capsules                      |
| Investigational medicinal product code | R05CA13                                      |
| Other name                             | German original name: Soledum® Kapseln forte |
| Pharmaceutical forms                   | Gastro-resistant capsule, soft               |
| Routes of administration               | Oral use                                     |

**Dosage and administration details:**

The IMP will be administered at home three times a day (morning, noon, evening, t.i.d.: 3x1 capsules). Treatment starts on the day of Visit 2 (Day 1) at the trial site and ends on the day of Visit 4 (Day 15±2) at home. Subjects, who recover from common cold before Visit 4, may terminate the administration of the IMP, once the first 10 WURSS-11 questions were rated by the subject "0" on two consecutive assessments in the eDiary.

On Day 1 (start of treatment), the IMP will be administered once (1x1 capsule), twice (2x1 capsule) or three times (3x1 capsule) by the subject depending on the time of Visit 2. On the day of Visit 4 (Day 15±2), the IMP will only be administered once in the morning (1x1 capsule, last dose).

IMP has to be swallowed unchewed with sufficient fluid (preferably one glass of water [200 mL]), but no hot beverage, approximately half an hour before a meal. Subjects with a sensitive stomach are recommended to take the IMP during their regular meals.

|                  |       |
|------------------|-------|
| <b>Arm title</b> | >24 h |
|------------------|-------|

**Arm description:**

Time to treatment stratum >24 h

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Soledum® forte capsules                      |
| Investigational medicinal product code | R05CA13                                      |
| Other name                             | German original name: Soledum® Kapseln forte |
| Pharmaceutical forms                   | Gastro-resistant capsule, soft               |
| Routes of administration               | Oral use                                     |

**Dosage and administration details:**

The IMP will be administered at home three times a day (morning, noon, evening, t.i.d.: 3x1 capsules). Treatment starts on the day of Visit 2 (Day 1) at the trial site and ends on the day of Visit 4 (Day 15±2) at home. Subjects, who recover from common cold before Visit 4, may terminate the administration of the IMP, once the first 10 WURSS-11 questions were rated by the subject "0" on two consecutive assessments in the eDiary.

On Day 1 (start of treatment), the IMP will be administered once (1x1 capsule), twice (2x1 capsule) or three times (3x1 capsule) by the subject depending on the time of Visit 2. On the day of Visit 4 (Day 15±2), the IMP will only be administered once in the morning (1x1 capsule, last dose).

IMP has to be swallowed unchewed with sufficient fluid (preferably one glass of water [200 mL]), but no hot beverage, approximately half an hour before a meal. Subjects with a sensitive stomach are recommended to take the IMP during their regular meals.

**Notes:**

[2] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is the screening phase and therefore not the baseline period.

| <b>Number of subjects in period 3<sup>[3]</sup>[4]</b> | ≤12 h | >12 to 24 h | >24 h |
|--|-------|-------------|-------|
| Started  | 122   | 88          | 98    |
| Completed  | 122   | 88          | 98    |

**Notes:**

[3] - 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: The enrolled patients were first in the screening phase and only a part of them became ill and entered the baseline period.

[4] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same

as the number completing the preceding period.

Justification: Not all patients fulfilled the criteria to enter the next period.

## Baseline characteristics

### Reporting groups

|                                       |             |
|---------------------------------------|-------------|
| Reporting group title                 | ≤12 h       |
| Reporting group description:          |             |
| Time to treatment stratum ≤12 h       |             |
| Reporting group title                 | >12 to 24 h |
| Reporting group description:          |             |
| Time to treatment stratum >12 to 24 h |             |
| Reporting group title                 | >24 h       |
| Reporting group description:          |             |
| Time to treatment stratum >24 h       |             |

| Reporting group values                                     | ≤12 h    | >12 to 24 h | >24 h    |
|--|----------|-------------|----------|
| Number of subjects   | 122      | 88          | 98       |
| Age categorical  |          |             |          |
| Units: Subjects  |          |             |          |
| In utero   |          |             |          |
| Preterm newborn infants (gestational age < 37 wks)         |          |             |          |
| Newborns (0-27 days)                                       |          |             |          |
| Infants and toddlers (28 days-23 months)                   |          |             |          |
| Children (2-11 years)                                      |          |             |          |
| Adolescents (12-17 years)                                  |          |             |          |
| Adults (18-64 years)                                       |          |             |          |
| From 65-84 years   |          |             |          |
| 85 years and over  |          |             |          |
| Age continuous   |          |             |          |
| Units: years   |          |             |          |
| arithmetic mean  | 37.9     | 38.4        | 39.8     |
| full range (min-max)                                       | 18 to 70 | 18 to 69    | 18 to 69 |
| Gender categorical   |          |             |          |
| Units: Subjects  |          |             |          |
| Female   | 86       | 52          | 53       |
| Male   | 36       | 36          | 45       |
| Smoking status   |          |             |          |
| Units: Subjects  |          |             |          |
| Non-smoker   | 87       | 64          | 73       |
| Ex-smoker  | 13       | 0           | 5        |
| Smoker   | 22       | 24          | 20       |
| Working status   |          |             |          |
| Units: Subjects  |          |             |          |
| (Self-) employed   | 94       | 66          | 79       |
| Not employed   | 12       | 11          | 4        |
| Student  | 16       | 11          | 15       |
| Influenza vaccination for the coming/current winter season |          |             |          |
| Units: Subjects  |          |             |          |
| No   | 98       | 72          | 87       |



|   |             |             |             |
|---|-------------|-------------|-------------|
| Yes   | 24          | 16          | 11          |
| Race  |             |             |             |
| Units: Subjects                             |             |             |             |
| Caucasian (white)                           | 120         | 85          | 98          |
| Black                                       | 1           | 2           | 0           |
| Other                                       | 1           | 1           | 0           |
| Alcohol consumption                         |             |             |             |
| Units: Subjects                             |             |             |             |
| None  | 90          | 72          | 66          |
| Low level consumption                       | 15          | 6           | 7           |
| Substantial consumption                     | 17          | 10          | 25          |
| Common cold episodes during previous winter |             |             |             |
| September to March (number)                 |             |             |             |
| Units: number                               |             |             |             |
| median                                      | 2.0         | 2.0         | 2.0         |
| full range (min-max)                        | 1 to 7      | 1 to 10     | 1 to 5      |
| Baseline WURSS score                        |             |             |             |
| Units: number                               |             |             |             |
| arithmetic mean                             | 27.31       | 29.30       | 26.80       |
| full range (min-max)                        | 3.0 to 57.0 | 6.0 to 54.0 | 4.0 to 53.0 |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>                      | Total |  |  |
| Number of subjects                                 | 308   |  |  |
| 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)                               | 0     |  |  |
| From 65-84 years                                   | 0     |  |  |
| 85 years and over                                  | 0     |  |  |
| Age continuous                                     |       |  |  |
| Units: years                                       |       |  |  |
| arithmetic mean                                    |       |  |  |
| full range (min-max)                               | -     |  |  |
| Gender categorical                                 |       |  |  |
| Units: Subjects                                    |       |  |  |
| Female   | 191   |  |  |
| Male   | 117   |  |  |
| Smoking status                                     |       |  |  |
| Units: Subjects                                    |       |  |  |
| Non-smoker   | 224   |  |  |
| Ex-smoker  | 18    |  |  |
| Smoker   | 66    |  |  |
| Working status                                     |       |  |  |
| Units: Subjects                                    |       |  |  |

|   |     |  |  |
|---|-----|--|--|
| (Self-) employed  | 239 |  |  |
| Not employed  | 27  |  |  |
| Student   | 42  |  |  |
| Influenza vaccination for the coming/current winter season<br>Units: Subjects |     |  |  |
| No  | 257 |  |  |
| Yes   | 51  |  |  |
| Race<br>Units: Subjects   |     |  |  |
| Caucasian (white)   | 303 |  |  |
| Black   | 3   |  |  |
| Other   | 2   |  |  |
| Alcohol consumption<br>Units: Subjects  |     |  |  |
| None  | 228 |  |  |
| Low level consumption   | 28  |  |  |
| Substantial consumption   | 52  |  |  |
| Common cold episodes during previous winter<br>September to March (number)    |     |  |  |
| Units: number   |     |  |  |
| median  |     |  |  |
| full range (min-max)  | -   |  |  |
| Baseline WURSS score<br>Units: number   |     |  |  |
| arithmetic mean   |     |  |  |
| full range (min-max)  | -   |  |  |

### Subject analysis sets

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | mITT                        |
| Subject analysis set type  | Modified intention-to-treat |

Subject analysis set description:

Modified intention-to-treat set (mITT) comprised all subjects:

- who received at least 4 IMP doses within the first 4 days after Visit 2 with maximum one day without treatment;
- who provided at least 5 valid WURSS-11 assessments within the first 7 days after symptom onset with a maximum of 2 days without assessment;
- without intake of antibiotics after start of IMP treatment due to symptoms associated with upper respiratory tract infections.

The mITT was used for the identification of potential confounders and for the evaluation of primary and secondary endpoints in a more "real-life" setting.

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | SAF             |
| Subject analysis set type  | Safety analysis |

Subject analysis set description:

Safety Set (SAF) included all subjects, who received at least one dose of the IMP. The SAF was used for analysis of safety and tolerability.

| Reporting group values | mITT | SAF |  |
|------------------------|------|-----|--|
| Number of subjects     | 308  | 329 |  |

|  |          |  |  |
|--|----------|--|--|
| Age categorical<br>Units: Subjects   |          |  |  |
| In utero<br>Preterm newborn infants<br>(gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |          |  |  |
| Age continuous<br>Units: years   |          |  |  |
| arithmetic mean  | 38.7     |  |  |
| full range (min-max)   | 18 to 70 |  |  |
| Gender categorical<br>Units: Subjects  |          |  |  |
| Female   | 191      |  |  |
| Male   | 117      |  |  |
| Smoking status<br>Units: Subjects  |          |  |  |
| Non-smoker   | 224      |  |  |
| Ex-smoker  | 18       |  |  |
| Smoker   | 66       |  |  |
| Working status<br>Units: Subjects  |          |  |  |
| (Self-) employed   | 239      |  |  |
| Not employed   | 27       |  |  |
| Student  | 42       |  |  |
| Influenza vaccination for the coming/current winter season<br>Units: Subjects  |          |  |  |
| No   | 257      |  |  |
| Yes  | 51       |  |  |
| Race<br>Units: Subjects  |          |  |  |
| Caucasian (white)  |          |  |  |
| Black  |          |  |  |
| Other  |          |  |  |
| Alcohol consumption<br>Units: Subjects   |          |  |  |
| None   |          |  |  |
| Low level consumption  |          |  |  |
| Substantial consumption  |          |  |  |
| Common cold episodes during previous winter  |          |  |  |
| September to March (number)  |          |  |  |
| Units: number  |          |  |  |
| median   | 2.0      |  |  |
| full range (min-max)   | 1 to 10  |  |  |
| Baseline WURSS score   |          |  |  |

|                      |             |  |  |
|----------------------|-------------|--|--|
| Units: number        |             |  |  |
| arithmetic mean      | 27.71       |  |  |
| full range (min-max) | 3.0 to 57.0 |  |  |

## End points

### End points reporting groups

|  |                             |
|--|-----------------------------|
| Reporting group title  | Screening Phase             |
| Reporting group description: -   |                             |
| Reporting group title  | Onset of symptoms           |
| Reporting group description: -   |                             |
| Reporting group title  | ≤12 h                       |
| Reporting group description:   |                             |
| Time to treatment stratum ≤12 h  |                             |
| Reporting group title  | >12 to 24 h                 |
| Reporting group description:   |                             |
| Time to treatment stratum >12 to 24 h  |                             |
| Reporting group title  | >24 h                       |
| Reporting group description:   |                             |
| Time to treatment stratum >24 h  |                             |
| Subject analysis set title   | mITT                        |
| Subject analysis set type  | Modified intention-to-treat |
| Subject analysis set description:  |                             |
| Modified intention-to-treat set (mITT) comprised all subjects:   |                             |
| <ul style="list-style-type: none"><li>• who received at least 4 IMP doses within the first 4 days after Visit 2 with maximum one day without treatment;</li><li>• who provided at least 5 valid WURSS-11 assessments within the first 7 days after symptom onset with a maximum of 2 days without assessment;</li><li>• without intake of antibiotics after start of IMP treatment due to symptoms associated with upper respiratory tract infections.</li></ul> |                             |
| The mITT was used for the identification of potential confounders and for the evaluation of primary and secondary endpoints in a more “real-life” setting.   |                             |
| Subject analysis set title   | SAF                         |
| Subject analysis set type  | Safety analysis             |
| Subject analysis set description:  |                             |
| Safety Set (SAF) included all subjects, who received at least one dose of the IMP. The SAF was used for analysis of safety and tolerability.   |                             |

### Primary: Area under the curve global symptom severity curve (AUC-WURSS) - LS Means

|  |   |
|--|---|
| End point title  | Area under the curve global symptom severity curve (AUC-WURSS) - LS Means |
| End point description:   |   |
| The primary efficacy endpoint was the Area under the curve global symptom severity (AUC-WURSS) using the primary efficacy variable subject-reported outcome WURSS-11.  |   |
| The derivation of AUC-WURSS was based on mean daily total WURSS-11 scores, which were derived by averaging evening assessment of considered symptom day and morning assessment of the subsequent day separately for each item. If only one of both assessments was available, this assessment was used as mean item score for a symptom day. |   |
| The mean item scores for questions 2 to 10 (daily single item scores) were then summed up to the mean total score of a day. Imputation of missing data was performed up to (estimated) day of recovery.  |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| The mean daily total scores (imputed) were summed up from Symptom Day 1 to Symptom Day 17 using trapezoidal approximation, which corresponds to a time frame of common cold onset to treatment day 15 (assuming treatment starts on Symptom Day 3  |   |

| End point values                             | ≤12 h                  | >12 to 24 h            | >24 h                  |  |
|--|------------------------|------------------------|------------------------|--|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed                  | 122                    | 88                     | 98                     |  |
| Units: AUC                                   |                        |                        |                        |  |
| least squares mean (confidence interval 95%) | 143.1 (117.7 to 168.5) | 181.6 (152.5 to 210.8) | 232.0 (203.4 to 260.5) |  |

## Statistical analyses

| Statistical analysis title   | GLM model                   |
|--|-----------------------------|
| Statistical analysis description:  |                             |
| Model contains time-to-treatment stratum, previous influenza vaccination, alcohol consumption, working status and categorized baseline WURSS-11 score. |                             |
| Comparison groups  | ≤12 h v >12 to 24 h v >24 h |
| Number of subjects included in analysis  | 308                         |
| Analysis specification   | Pre-specified               |
| Analysis type  | superiority                 |
| P-value  | < 0.0001 <sup>[1]</sup>     |
| Method   | ANCOVA                      |

Notes:

[1] - Effect time to treatment stratum.

## Primary: Area under the curve global symptom severity curve (AUC-WURSS) LS means difference

| End point title                               | Area under the curve global symptom severity curve (AUC-WURSS) LS means difference <sup>[2][3]</sup> |
|---|--|
| End point description:                        |  |
| Below the LS means difference were presented. |  |
| End point type                                | Primary  |

End point timeframe:

The mean daily total scores (imputed) were summed up from Symptom Day 1 to Symptom Day 17 using trapezoidal approximation, which corresponds to a time frame of common cold onset to treatment day 15 (assuming treatment starts on Symptom Day 3).

Notes:

[2] - 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: It is the same statistical analysis as for the other primary endpoint.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This is due to the LS means difference. The results show the difference to the third arm.

| End point values                             | ≤12 h                   | >12 to 24 h            |  |  |
|--|-------------------------|------------------------|--|--|
| Subject group type                           | Reporting group         | Reporting group        |  |  |
| Number of subjects analysed                  | 122                     | 88                     |  |  |
| Units: AUC LS means difference               |                         |                        |  |  |
| least squares mean (confidence interval 95%) | -88.9 (-118.0 to -59.8) | -50.3 (-82.0 to -18.7) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Course of mean daily total score:

|                 |                                   |
|-----------------|-----------------------------------|
| End point title | Course of mean daily total score: |
|-----------------|-----------------------------------|

End point description:

Mean daily total scores were derived per Symptom Day as described for the primary efficacy endpoint and were analysed per symptom day.

Due to abundance of data for this secondary endpoint only the data of first symptom day is presented, data for all symptom days are presented in the enclosed graph in the attachment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Course of mean daily total scores from common cold onset to end-of-trial.

| End point values                             | ≤12 h                  | >12 to 24 h            | >24 h                  |  |
|--|------------------------|------------------------|------------------------|--|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed                  | 122                    | 88                     | 98                     |  |
| Units: WURSS-11 mean daily total score       |                        |                        |                        |  |
| least squares mean (confidence interval 95%) | 27.61 (25.73 to 29.49) | 28.87 (26.67 to 31.07) | 28.65 (26.55 to 30.76) |  |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | MMRM Model 2 for WURSS-11 mean daily total score/Figure |
|-----------------------------------|---|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Course of mean daily QoL score

|                 |                                |
|-----------------|--------------------------------|
| End point title | Course of mean daily QoL score |
|-----------------|--------------------------------|

End point description:

Mean daily group scores were derived analogously to mean daily total score by considering only WURSS-11 questions 2 to 8 for the symptom domain (i.e., aggregated for nasal, throat and item feeling tired) and WURSS-11 questions 9 and 10 for the QoL domain.

Due to the abundance of data only the data of first symptom day is presented, all symptom day data is presented in the enclosed graph in the attachment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Course of mean daily QoL scores from common cold onset to end-of-trial.

| End point values                             | ≤12 h               | >12 to 24 h         | >24 h               |  |
|--|---------------------|---------------------|---------------------|--|
| Subject group type                           | Reporting group     | Reporting group     | Reporting group     |  |
| Number of subjects analysed                  | 122                 | 88                  | 98                  |  |
| Units: Scores                                |                     |                     |                     |  |
| least squares mean (confidence interval 95%) | 6.07 (5.49 to 6.65) | 6.03 (5.35 to 6.72) | 6.23 (5.57 to 6.88) |  |

|                            |   |
|----------------------------|---|
| Attachments (see zip file) | MMRM Model 2 for WURSS-11 mean daily QoL Score/Figure |
|----------------------------|---|

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to remission

|                 |                   |
|-----------------|-------------------|
| End point title | Time to remission |
|-----------------|-------------------|

End point description:

Remission was considered as present, if daily single item score of WURSS-11 question 1 was ≤1 together with only one symptom scored ≤3 and all other symptoms scored 0 of the considered day based on corresponding single item scores.

Time to remission was then defined as the symptom day of first documented remission. A subject was censored at the time of last measurement if no remission was observed before.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From common cold onset to end-of-trial.

| End point values                | ≤12 h           | >12 to 24 h     | >24 h           | mITT                 |
|---------------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type              | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed     | 122             | 88              | 98              | 308                  |
| Units: Time to remission (days) |                 |                 |                 |                      |
| median (full range (min-max))   | 9.0 (3 to 18)   | 10.0 (6 to 18)  | 11.0 (5 to 18)  | 10.0 (3 to 18)       |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Incidence of AEs - related, not related to IMP

|                 |  |
|-----------------|--|
| End point title | Incidence of AEs - related, not related to IMP |
|-----------------|--|



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**End point description:**

The number of AEs and the number and percentage of subjects with at least one AE were tabulated by MedDRA system organ class (SOC) and preferred term (PT).

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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**End point timeframe:**

Start of IMP intake at visit 2, ends at last study visit per subject. If the investigator becomes aware of an AE up to one week after the administration of the last IMP / rescue medication intake this has also to be documented.

---

|                             |                      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| <b>End point values</b>     | SAF                  |  |  |  |
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 329                  |  |  |  |
| Units: Numnber of AEs       |                      |  |  |  |
| number (not applicable)     |                      |  |  |  |
| Related                     | 17                   |  |  |  |
| Not related                 | 8                    |  |  |  |
| Total                       | 25                   |  |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

AE recording started after first IMP administration and ended at last trial visit per subject, related AEs 1 week after last intake. Not recovered AEs were to be followed up until resolved or stabilized so that no further improvement could be expected.

Adverse event reporting additional description:

At each visit, the investigator assessed by asking an open standard question (Have anything changed in your state of health since you last came to see me?) if any AEs (non-serious and serious) had occurred. Any AEs, spontaneously reported by the subject or by the subject's relatives/delegates or observed by the investigator were to be recorded.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 23.0   |

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Safety Set |
|-----------------------|------------|

Reporting group description:

Safety set (SAF) included all subjects, who received at least one dose of the IMP. The SAF was used for analysis of safety and tolerability.

| Serious adverse events                            | Safety Set      |  |  |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 0 / 329 (0.00%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | Safety Set      |  |  |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 0 / 329 (0.00%) |  |  |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The threshold to report non-serious adverse events is 5%. None of the non-serious AEs had a frequency of 5% or more.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 18 November 2020 | <p>Amendment 1 introduced the rapid antigen SARS-CoV-2 test as alternative to the PCR test.</p> <p>During the trial, new test methods for SARS-CoV-2 had been established, i.e., an antigen rapid test became commercially available on the market. To allow the sites also to use this antigen rapid test as an alternative to the already implemented PCR-test, this protocol amendment became necessary. The sites could use either the PCR test or the antigen rapid test. The advantage of the antigen rapid test was, that the result was available within a couple of minutes and a decision of exclusion of subject from further trial participation could be made immediately. Furthermore, the currently limited test capacities for PCR test were not blocked for trial purposes. This change was considered as a substantial change to the protocol.</p> <p>In parallel, some other minor protocol specifications were also changed (non-substantial).</p> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported