# Clinical trial results:
# Patient-controlled sedation with propofol versus combined sedation during bronchoscopy – a randomized controlled trial

## Summary

| | |
|---|---|
| EudraCT number | 2015-005274-38 |
| Trial protocol | SE |
| Global end of trial date | 09 May 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 26 December 2021 |
| First version publication date | 26 December 2021 |
| Summary attachment (see zip file) | Published article (Patient_controlled_Sedation_During_Flexible.3.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | BRONSE |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03357393 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Universitetssjukhuset i Linköping |
| Sponsor organisation address | Universitetssjukhuset, Linköping, Sweden, 58185 |
| Public contact | Universitetssjukhuset i Linköping, Region Östergötland, lena.nilsson@regionostergotland.se |
| Scientific contact | Universitetssjukhuset i Linköping, Region Östergötland, lena.nilsson@regionostergotland.se |

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 | 03 January 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 09 May 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

We hypothesise that the use of propofol patient controlled sedation for outpatient bronchoscopy will be a safe and well accepted procedure by patients and bronchoscopists, and increase the amount of patients ready for discharge after two hours, compared with sedation using midazolam and morphine.

Protection of trial subjects:

If patient is randomized to sedation with PCS the nurse anaesthetist will give additional thorough information and instructions how to operate the PCS device before premedication is administrated and the bronchoscopy begins.

A nurse anaesthetist is present during the whole procedure until sedation level OAA/S 5 is reached, thereafter and before procedure a pulmonary nurse is present. Bronchoscopist and anaesthesiologist are available via telephone and/or pager and can be present within a few minutes. All of the drugs are administered by routes and given in doses in accordance with approval from the Swedish Medical Products Agency. The personnel involved in the procedure are all familiar with the use of the drugs being studied.

During the procedure the anaesthesiologist is available for consultation via telephone and will be informed before sedation and bronschoscopy procedure begins. Furthermore the anaesthesiologist is available within minutes if call is made to anaesthesiologist pager. Before bronchoscopy is initiated (one hour after premedication) the patient is encouraged to start using the PCS until the patient feel comfortable. At the same time local anaesthetic is administrated nasally and pharyngeally depending on type of bronchoscopy and during the procedure local anaesthetic is administrated with a spray-as- you-go technique to anaesthetize vocal cords and trachea. During the procedure the bronchoscopist may request additional medication to achieve deeper sedation and/or pain relief due to a need that the patient has to be completely still during specially demanding and potentially dangerous parts of the procedure. If requested, the sedation is deepened with additional midazolam (if group MM) by nurse anaesthetist or by awaiting the PCS to deliver additional requests from the patient (if group MP or GP). If pain relief is needed additional topical anaesthetics is administrated by bronchoscopist and/or alfentanil (rescue).

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 March 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Sweden: 150 |
| Worldwide total number of subjects | 150 |
| EEA total number of subjects | 150 |

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) | 53 |
| From 65 to 84 years | 95 |
| 85 years and over | 2 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted following the principles of the amended Declaration of Helsinki at the Department of Pulmonary Medicine, Linköping University Hospital, from April 2016 to May 2017.

### Pre-assignment

Screening details:

Exclusion criteria:positive pregnancy test, contraindication for the study drugs, functional disability, and cognitive impairment or language difficulties).
185 screened.
35 excluded (cancelled FB, 17 declined to participate, 3 contraindication, 5 cognitive disability, 3 personnel not available, 2 exclusion note missing)

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

The bronchoscopist was blinded to the premedication, and it was administered by the bronchoscopic team.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Control group |

Arm description:

Morphine-scopolamine/midazolam (NCS)

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Morphine-scopolamine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Morphine-scopolamine by age (18 to 54 y, 1.0 mL; 55 to 65 y, 0.75 mL; above 65 y, 0.5mL),

| | |
|---|---|
| Investigational medicinal product name | Midazolam |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for injection |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

Initial dose of 1.25mg of midazolam and, when necessary, repeated doses of 1.25mg, according to the type of procedure or bronchoscopist request.

| | |
|---|---|
| **Arm title** | Intervention group (PCS-MS) |

Arm description:

Morphine-scopolamine/propofol (PCS)

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Morphine-scopolamine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection/infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Morphine-scopolamine by age (18 to 54 y, 1.0 mL; 55 to 65 y, 0.75 mL; above 65 y, 0.5mL),

| | |
|---|---|
| Investigational medicinal product name | Propofol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Concentrate for solution for infusion |

Dosage and administration details:

By pressing a button, patients could self-administer a bolus of 5mg of propofol (0.5 mL) without lockout periods. The delivery time was 8 seconds, with an estimated maximum of 35mg of propofol/min if the patient were to repeatedly press the button for boluses.

| | |
|---|---|
| **Arm title** | Intervention group (PCS-G) |

Arm description:

Glycopyrrolate/propofol (PCS)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Glycopyrrolate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Glycopyrronium 0.2mg.

| | |
|---|---|
| Investigational medicinal product name | Propofol |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Concentrate for solution for infusion |

Dosage and administration details:

By pressing a button, patients could self-administer a bolus of 5mg of propofol (0.5 mL) without lockout periods. The delivery time was 8 seconds, with an estimated maximum of 35mg of propofol/min if the patient were to repeatedly press the button for boluses.

| **Number of subjects in period 1** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) |
|---|---|---|---|
| Started | 50 | 50 | 50 |
| Completed | 50 | 50 | 50 |

## Baseline characteristics

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | Control group |
| Reporting group description: Morphine-scopolamine/midazolam (NCS) | |
| Reporting group title | Intervention group (PCS-MS) |
| Reporting group description: Morphine-scopolamine/propofol (PCS) | |
| Reporting group title | Intervention group (PCS-G) |
| Reporting group description: Glycopyrrolate/propofol (PCS) | |

| Primary: Discharge Assessment Using PADSS After 2 Hours Number of Patients Reaching PADSS Score 10 After 2 Hours | |
|---|---|
| End point title | Discharge Assessment Using PADSS After 2 Hours Number of Patients Reaching PADSS Score 10 After 2 Hours |
| End point description: ost Anaesthetic Discharge Scoring System (PADSS).A measurement of the PADSS score is done by pulmonary nurse every 15 min after bronchoscopy is finished (when bronchoscope is removed) for 2 hours. The PADSS is used to clinically assess if the patient is ready to be discharged after anaesthesia/sedation and consist of five criteria: vital signs, ambulation, nausea and/or vomiting, pain and surgical bleeding. Each criterion is given a score ranging from 0 to 2. Only patients who achieve a total score of 10 are considered ready for discharge after 2 hours. | |
| End point type | Primary |
| End point timeframe: 2 hours after bronchoscopy is finished | |

| End point values | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Participants | 19 | 30 | 45 | |

### Statistical analyses

| Statistical analysis title | Planned comparison PCS-MS vs PCS-G |
|---|---|
| Comparison groups | Intervention group (PCS-MS) v Intervention group (PCS-G) |
| Number of subjects included in analysis | 100 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | < 0.05 |
| Method | Planned comparison |

Notes:

[1] - The groups were compared using a planned comparison. First, the control group was compared with the combined 2 PCS groups. Second, the PCS-MS group was compared with the PCS-G Group.

| **Statistical analysis title** | Planned comparison Control vs PCS-MS/PCS-G |
|---|---|
| Comparison groups | Control group v Intervention group (PCS-MS) v Intervention group (PCS-G) |
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[2] |
| P-value | < 0.05 |
| Method | Planned comparison |

Notes:

[2] - The groups were compared using a planned comparison. First, the control group was compared with the combined 2 PCS groups. Second, the PCS-MS group was compared with the PCS-G Group.

## Secondary: Assessment of Self-rated Patient Questionaries' Using S-PSR

| End point title | Assessment of Self-rated Patient Questionaries' Using S-PSR |
|---|---|

End point description:

Post-discharge Surgical Recovery Scale (S-PSR) The modified Swedish version S-PSR is based on the "Post-discharge Surgical Recovery Scale" and is a 14-item questionnaire to assess the recovery post-discharge regarding the patients' health status and activity (see further appendix 2). Each item is rated using a semantic differential scale and the total sum is multiplied by 100. The possible range is 10-100, with higher score indicating a more favourable postoperative recovery.

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

End point timeframe:

The assessment is done by the patient at home (or at ward if pro-longed hospital stay is necessary) in the evening on the day of bronchoscopy. It takes approximately 2 minutes to complete the questionnaire.

| **End point values** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Units on a scale | | | | |
| median (full range (min-max)) | 55 (36 to 77) | 56 (43 to 73) | 54 (41 to 100) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Quality of Recovery (QoR-23)

| End point title | Quality of Recovery (QoR-23) |
|---|---|

End point description:

Modified version of Quality of Recovery (QoR-23) Minimum value 23. Maximum value 115. A higher score indicate a better quality of recovery.
The questionnaire "Quality of Recovery" (QoR-23) is a 23 item questionnaire to assess recovery after day surgery regarding the patients' emotional state, physical comfort and physical independence (see further appendix 4). Each item is rated on a five-point scale (1-5) and the scores are summed.

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

End point timeframe:

The assessment is done by the patient at home (or at ward if pro-longed hospital stay is necessary) in the morning the day after bronchoscopy. It takes less than 1 minute to complete the assessment.

| **End point values** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Score on a scale | | | | |
| median (full range (min-max)) | 100 (61 to 112) | 102 (60 to 115) | 100 (63 to 115) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Patients' Satisfaction Using a Likert-type Scale

| End point title | Patients' Satisfaction Using a Likert-type Scale |
|---|---|

End point description:

overall satisfaction with the procedure using the Likert-type scale (1. Very dissatisfied, 2. Dissatisfied, 3. Neither satisfied nor dissatisfied, 4. Satisfied, 5. Very satisfied). The patient may comment any cause which made the satisfaction score high or low and if the patient would like to receive the same method of sedation during a future bronchoscopy.

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

End point timeframe:

After patient has recovered after bronchoscopy and before discharge home, estimated period of time 0-24 hours.

| **End point values** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Units on a scale | | | | |
| median (full range (min-max)) | 5 (2 to 5) | 5 (4 to 5) | 5 (4 to 5) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Bronchoscopist Evaluation Using a Likert-type Scale

| End point title | Bronchoscopist Evaluation Using a Likert-type Scale |
|---|---|

End point description:

The bronchoscopist assess their perception of cough, bronchial secretion respectively circumstances for a smooth performance of the bronchoscopy of procedure using the Likert-type scale (1. Very dissatisfied, 2. Dissatisfied, 3. Neither satisfied nor dissatisfied, 4. Satisfied, 5. Very satisfied).

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

End point timeframe:

Directly after completion of the procedure.

| **End point values** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Units on a scale | | | | |
| median (full range (min-max)) | 5 (2 to 5) | 4 (1 to 5) | 4 (2 to 5) | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Level of Sedation Using the Observer's Assessment of Alertness/Sedation (OAA/S) Scale**

| End point title | Level of Sedation Using the Observer's Assessment of Alertness/Sedation (OAA/S) Scale |
|---|---|

End point description:

Level of sedation is assessed every 5th minute during the procedure by the nurse anaesthetist using The Observer's Assessment of Alertness/Sedation (OAA/S) scale whereby a higher score represent a lighter sedation. Below is the scale descriped, Observation/score:
Responds readily to name spoken in normal tone/5 Lethargic response to name spoken in normal tone/4 Responds only after name is called loudly and/or repeatedly/3 Responds only after mild prodding or shaking/2 Does not respond to mild prodding or shaking/1

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

End point timeframe:

Assessement are done every 5th minute from procedure start until end of procedure (extraction of bronchoscope), estimated period of time 0-60 minutes.

| **End point values** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Units on a scale | | | | |
| median (full range (min-max)) | 3 (1 to 4) | 2 (1 to 4) | 2 (1 to 4) | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Number of Participants With Interventions Performed

| End point title | Number of Participants With Interventions Performed |
|---|---|

End point description:

Number of participants with interventions performed to maintain cardiovascular (if atropine or ephidrine has been given) and respiratory stability (if assisted ventilation, chin lift or painful stimulation has been performed). Assesed every five minutes during the procedure.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

From procedure start until end of procedure (extraction of bronchoscope), estimated period of time 0-60 minutes.

| End point values | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Participants | 1 | 4 | 3 | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Arterial Oxygen Saturation (SpO2)

| End point title | Arterial Oxygen Saturation (SpO2) |
|---|---|

End point description:

Outcome Measure Data Reported for participants SpO2 < 90%

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Every five minutes during the procedure (from procedure start until end of procedure (extraction of bronchoscope), , estimated period of time 0-60 minutes, and thereafter after the procedure every 15 minutes until PADSS score ≥9 or maximum 4 hours.

| End point values | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Participants | 4 | 4 | 7 | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Respiratory Rate Per Minute (RR)

| End point title | Respiratory Rate Per Minute (RR) |
|---|---|

End point description:

Outcome Measure Data Reported for participants RR<8 breaths/min

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Every five minutes during the procedure (from procedure start until end of procedure (extraction of bronchoscope), , estimated period of time 0-60 minutes, and thereafter after the procedure every 15 minutes until PADSS score ≥9 or maximum 4 hours.

| End point values | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Participants | 4 | 6 | 2 | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Non-invasive Blood Pressure (NIBP)

| End point title | Non-invasive Blood Pressure (NIBP) |
|---|---|

End point description:

Outcome Measure Data Reported for participants NIBP <90mmHg

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Every five minutes during the procedure (from procedure start until end of procedure (extraction of bronchoscope), , estimated period of time 0-60 minutes, and thereafter after the procedure every 15 minutes until PADSS score ≥9 or maximum 4 hours.

| End point values | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Participants | 2 | 2 | 2 | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Heart Rate (Beats Per Minute, HR)

| End point title | Heart Rate (Beats Per Minute, HR) |
|---|---|

End point description:

Outcome Measure Data Reported for participants HR<40 beats/min

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Every five minutes during the procedure (from procedure start until end of procedure (extraction of bronchoscope), , estimated period of time 0-60 minutes, and thereafter after the procedure every 15 minutes until PADSS score ≥9 or maximum 4 hours.

| **End point values** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 50 | 50 | 50 | |
| Units: Participants | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start preparation for bronchospcpy (first drug given) to completing the questionnary QoR-23 on the day after procedure

Adverse event reporting additional description:

In the incident report the following grading is used to rate the severity of an incidence:
Mild = aware of the symptoms but they are tolerable
Moderate = symptoms partially affect daily activities
Severe = symptoms significantly affect daily activities
The investigator assesses the relationship between the incidence and the study, as defined:

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

### Dictionary used

| | |
|---|---|
| Dictionary name | Clinic specific |
| Dictionary version | 1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Control group |
| Reporting group description: - | |
| Reporting group title | Intervention group (PCS-MS) |
| Reporting group description: - | |
| Reporting group title | Intervention group (PCS-G) |

Reporting group description: -

| Serious adverse events | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 0 / 50 (0.00%) | 1 / 50 (2.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Overnight admission | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 0 / 50 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 6 / 6 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | Control group | Intervention group (PCS-MS) | Intervention group (PCS-G) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 6 / 50 (12.00%) | 2 / 50 (4.00%) |
| Cardiac disorders | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all) | 0 | 0 | 2 |
| General disorders and administration site conditions | | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 6 / 50 (12.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 6 | 12 | 0 |
| Fever | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 0 / 50 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all) | 0 | 0 | 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

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/31478938