



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
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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 bronchoscopy 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)
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Arm description:

Morphine-scopolamine/propofol (PCS)

Arm type	Experimental
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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)
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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 Questionnaires' Using S-PSR

End point title	Assessment of Self-rated Patient Questionnaires' 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
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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 described, 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
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End point description:

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

End point type	Other pre-specified
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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)
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End point description:

Outcome Measure Data Reported for participants SpO2 < 90%

End point type	Other pre-specified
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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)
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End point description:

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

End point type	Other pre-specified
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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)
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End point description:

Outcome Measure Data Reported for participants NIBP <90mmHg

End point type	Other pre-specified
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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)
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End point description:

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

End point type	Other pre-specified
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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 bronchoscopy (first drug given) to completing the questionnaire 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
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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>