Clinical trial results:
Neuroplasticity induced by general anaesthesia

Summary

EudraCT number	2018-001252-35
Trial protocol	DK
Global end of trial date	13 August 2021

Results information

Result version number	v1 (current)
This version publication date	01 March 2025
First version publication date	01 March 2025

Trial information

Trial identification

Sponsor protocol code	DANA-2018-1.

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04125121
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Valdemar Hansens Vej 15, Glostrup, Denmark, DK-2600
Public contact	Glostrup, Rigshospitalet, signe.sloth.madsen@regionh.dk
Scientific contact	Glostrup, Rigshospitalet, +45 38633156, signe.sloth.madsen@regionh.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2021
Global end of trial reached?	Yes
Global end of trial date	13 August 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To explore and compare possible the de novo neuroplastic changes (visualised by magnetic resonnance imaging (MRI)) induced by anaesthesia with a volatile agent (sevoflurane) and total intravenous anaesthesia (propofol) respectively.

Protection of trial subjects:

Any condition (or history thereof) that could cause or be suspected to cause contraindications for general anaesthesia or magnetic resonance imaging led to non-inclusion or exclusion from the trial. Participants could withdraw from participation at any time without having to state a reason for cessation of participation. The participants could contact the principal investigator directly by phone call, text message or e-mail, and were encouraged to do so in case of any question or concern at any time throughout their participation. Inclusion and exclusion criteria were revisited with the participants before each session in the study, and informed consent was reconfirmed before intervention (general anaesthesia). The comfort and safety of the participants were first priority in all aspects of this trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	23
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited in Denmark via online advertising and in magazines for medical students in Copenhagen. Information and screening of applicants for eligibility, physical examinations, and obtainment of informed consent as was carried out by a physician at Rigshospitalet Glostrup, Denmark.

Pre-assignment

Screening details:

For detailed inclusion and exclusion criteria, please refer to www.clinicaltrials.gov, trial ID NCT04125121, and protocol article published in Trials 2020: DOI 10.1186/s13063-020-04468-y. Recruitment, screening and inclusion was carried out continuously throughout the trial period.

Period 1

Period 1 title	Overall trial period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	No
Arm title	Sevoflurane

Arm description:

1. Confirmation of eligibility for participation.
2. Baseline magnetic resonance imaging.
3. Intervention: Two hours of general anaesthesia with sevoflurane.
4. Magnetic resonance imaging four hours after general anaesthesia with sevoflurane.
5. Magnetic resonance imaging one day after general anaesthesia with sevoflurane.
6. Magnetic resonance imaging eight days after general anaesthesia with sevoflurane.

Questionnaires, cognitive testing and blood sampling was carried out corresponding to each MRI scan.

Arm type	Active comparator
Investigational medicinal product name	Sevoflurane
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, Medicinal gas, liquefied
Routes of administration	Inhalation use

Dosage and administration details:

Two hours of general anaesthesia with sevoflurane, minimum alveolar concentration (MAC) 1.5 or lower.

Arm title	Propofol

Arm description:

1. Confirmation of eligibility for participation.
2. Baseline magnetic resonance imaging.
3. Intervention: Two hours of general anaesthesia with propofol.
4. Magnetic resonance imaging four hours after general anaesthesia with propofol.
5. Magnetic resonance imaging one day after general anaesthesia with propofol.
6. Magnetic resonance imaging eight days after general anaesthesia with propofol.

Questionnaires, cognitive testing and blood sampling was carried out corresponding to each MRI scan.

Arm type	Active comparator
Investigational medicinal product name	Propofol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for infusion, Emulsion for injection
Routes of administration	Intravenous use

Dosage and administration details:

Two hours of general anaesthesia with propofol, infused with target controlled infusion using Schnider's pharmacokinetic model for propofol.

Number of subjects in period 1	Sevoflurane	Propofol
Started	21	22
Completed session 1	21	21
Ready for session 2 after wash-out	20	21
Completed session 2 (end of trial)	20	21
Completed	20	21
Not completed	1	1
Protocol deviation	1	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial period

Reporting group description:

23 subjects were included and proceeded to randomisation. After randomisation, two subjects were excluded due to protocol violation, and one subject withdrew from further participation after completing one arm (propofol). Thus, results from 21 subjects were included in further analysis from the propofol arm, while data from 20 subjects are included in the analysis from the sevoflurane arm, and two subjects appear at baseline while their data could not be used for further analysis.

Reporting group values	Overall trial period	Total	
Number of subjects	23	23	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Young adults (18-35 years)	23	23	
Age continuous			
Units: years			
arithmetic mean	23		
full range (min-max)	18 to 32	-	
Gender categorical			
Units: Subjects			
Female	13	13	
Male	10	10	

End points

End points reporting groups

Reporting group title	Sevoflurane

Reporting group description:

1. Confirmation of eligibility for participation.
2. Baseline magnetic resonance imaging.
3. Intervention: Two hours of general anaesthesia with sevoflurane.
4. Magnetic resonance imaging four hours after general anaesthesia with sevoflurane.
5. Magnetic resonance imaging one day after general anaesthesia with sevoflurane.
6. Magnetic resonance imaging eight days after general anaesthesia with sevoflurane.

Questionnaires, cognitive testing and blood sampling was carried out corresponding to each MRI scan.

Reporting group title	Propofol

Reporting group description:

1. Confirmation of eligibility for participation.
2. Baseline magnetic resonance imaging.
3. Intervention: Two hours of general anaesthesia with propofol.
4. Magnetic resonance imaging four hours after general anaesthesia with propofol.
5. Magnetic resonance imaging one day after general anaesthesia with propofol.
6. Magnetic resonance imaging eight days after general anaesthesia with propofol.

Questionnaires, cognitive testing and blood sampling was carried out corresponding to each MRI scan.

Primary: Sevoflurane, Whole brain volume, Baseline

End point title	Sevoflurane, Whole brain volume, Baseline[1][2]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[1] - 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: Optional

[2] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20[3]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1220 (± 112)			

Notes:

[3] - One participant was excluded after allocation to sevoflurane, 20 participants completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Whole brain volume, +4 hours

End point title	Sevoflurane, Whole brain volume, +4 hours[4][5]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with sevoflurane

Notes:

[4] - 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: Optional

[5] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20[6]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1220 (± 109)			

Notes:

[6] - One participant was excluded after allocation to sevoflurane, 20 participants completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Whole brain volume, +1 day

End point title	Sevoflurane, Whole brain volume, +1 day[7][8]

End point description:

End point type	Primary

End point timeframe:

+1 day after emergence from general anaesthesia with sevoflurane

Notes:

[7] - 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: Optional

[8] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20[9]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1215 (± 111)			

Notes:

[9] - One participant was excluded after allocation to sevoflurane, 20 participants completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Whole brain volume, +8 days

End point title	Sevoflurane, Whole brain volume, +8 days[10][11]

End point description:

End point type	Primary

End point timeframe:

+8 days after emergence from general anaesthesia with sevoflurane

Notes:

[10] - 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: Optional

[11] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20[12]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1213 (± 109)			

Notes:

[12] - One participant was excluded after allocation to sevoflurane, and 20 participants completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Grey matter volume, Baseline

End point title	Sevoflurane, Grey matter volume, Baseline[13][14]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[13] - 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: Optional

[14] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	697 (± 63)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Grey matter volume, +4 hours

End point title	Sevoflurane, Grey matter volume, +4 hours[15][16]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia

Notes:

[15] - 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: Optional

[16] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	696 (± 62)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Grey matter volume, +1 day

End point title	Sevoflurane, Grey matter volume, +1 day[17][18]

End point description:

End point type	Primary

End point timeframe:

+1 day after general anaesthesia with sevoflurane

Notes:

[17] - 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: Optional

[18] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	691 (± 63)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Grey matter volume, +8 days

End point title	Sevoflurane, Grey matter volume, +8 days[19][20]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with sevoflurane

Notes:

[19] - 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: Optional

[20] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	690 (± 60)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Hippocampus volume, Baseline

End point title	Sevoflurane, Hippocampus volume, Baseline[21][22]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[21] - 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: Optional

[22] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Hippocampus volume, +4 hours

End point title	Sevoflurane, Hippocampus volume, +4 hours[23][24]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia

Notes:

[23] - 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: Optional

[24] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Hippocampus volume, +1 day

End point title	Sevoflurane, Hippocampus volume, +1 day[25][26]

End point description:

End point type	Primary

End point timeframe:

+1 day after general anaesthesia with sevoflurane

Notes:

[25] - 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: Optional

[26] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Hippocampus volume, +8 days

End point title	Sevoflurane, Hippocampus volume, +8 days[27][28]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with sevoflurane

Notes:

[27] - 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: Optional

[28] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Thalamus volume, Baseline

End point title	Sevoflurane, Thalamus volume, Baseline[29][30]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[29] - 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: Optional

[30] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.8 (± 1.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Thalamus volume, +4 hours

End point title	Sevoflurane, Thalamus volume, +4 hours[31][32]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with sevoflurane

Notes:

[31] - 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: Optional

[32] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.7 (± 1.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Thalamus volume, +1 day

End point title	Sevoflurane, Thalamus volume, +1 day[33][34]

End point description:

End point type	Primary

End point timeframe:

+1 day after emergence from general anaesthesia with sevoflurane

Notes:

[33] - 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: Optional

[34] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.6 (± 1.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Thalamus volume, +8 days

End point title	Sevoflurane, Thalamus volume, +8 days[35][36]

End point description:

End point type	Primary

End point timeframe:

+8 days after emergence from general anaesthesia with sevoflurane

Notes:

[35] - 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: Optional

[36] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.7 (± 1.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Anterior Cingulate Cortex volume, Baseline

End point title	Sevoflurane, Anterior Cingulate Cortex volume, Baseline[37][38]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[37] - 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: Optional

[38] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.8 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Anterior Cingulate Cortex volume, +4 hours

End point title	Sevoflurane, Anterior Cingulate Cortex volume, +4 hours[39][40]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with sevoflurane

Notes:

[39] - 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: Optional

[40] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.8 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Anterior Cingulate Cortex volume, +1 day

End point title	Sevoflurane, Anterior Cingulate Cortex volume, +1 day[41][42]

End point description:

End point type	Primary

End point timeframe:

+1 day after general anaesthesia with sevoflurane

Notes:

[41] - 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: Optional

[42] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.8 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Sevoflurane, Anterior Cingulate Cortex volume, +8 days

End point title	Sevoflurane, Anterior Cingulate Cortex volume, +8 days[43][44]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with sevoflurane

Notes:

[43] - 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: Optional

[44] - 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: Optional

End point values	Sevoflurane			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.8 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Whole brain volume, Baseline

End point title	Propofol, Whole brain volume, Baseline[45][46]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[45] - 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: Optional

[46] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21[47]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1222 (± 108)			

Notes:

[47] - 22 participants were allocated to propofol, of which 1 was excluded and 21 completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Whole brain volume, +4 hours

End point title	Propofol, Whole brain volume, +4 hours[48][49]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with propofol

Notes:

[48] - 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: Optional

[49] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21[50]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1215 (± 108)			

Notes:

[50] - 22 participants were allocated to propofol, of which 1 was excluded and 21 completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Whole brain volume, +1 day

End point title	Propofol, Whole brain volume, +1 day[51][52]

End point description:

End point type	Primary

End point timeframe:

+1 day after general anaesthesia with propofol

Notes:

[51] - 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: Optional

[52] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21[53]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1216 (± 108)			

Notes:

[53] - 22 participants were allocated to propofol, of which 1 was excluded and 21 completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Whole brain volume, +8 days

End point title	Propofol, Whole brain volume, +8 days[54][55]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with propofol

Notes:

[54] - 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: Optional

[55] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21[56]			
Units: millilitre(s)				
arithmetic mean (standard deviation)	1216 (± 104)			

Notes:

[56] - 22 participants were allocated to propofol, of which 1 was excluded and 21 completed the arm.

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Grey matter volume

End point title	Propofol, Grey matter volume[57][58]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[57] - 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: Optional

[58] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	697 (± 59)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Grey matter volume, +4 hours

End point title	Propofol, Grey matter volume, +4 hours[59][60]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with propofol

Notes:

[59] - 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: Optional

[60] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	692 (± 59)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Grey matter volume, +1 day

End point title	Propofol, Grey matter volume, +1 day[61][62]

End point description:

End point type	Primary

End point timeframe:

+1 day after general anaesthesia with propofol

Notes:

[61] - 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: Optional

[62] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	691 (± 60)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Grey matter volume, +8 days

End point title	Propofol, Grey matter volume, +8 days[63][64]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with propofol

Notes:

[63] - 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: Optional

[64] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	692 (± 56)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Hippocampus volume, Baseline

End point title	Propofol, Hippocampus volume, Baseline[65][66]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[65] - 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: Optional

[66] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Hippocampus volume, +4 hours

End point title	Propofol, Hippocampus volume, +4 hours[67][68]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with propofol

Notes:

[67] - 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: Optional

[68] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Hippocampus volume, +1 day

End point title	Propofol, Hippocampus volume, +1 day[69][70]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with propofol

Notes:

[69] - 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: Optional

[70] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Hippocampus volume, +8 days

End point title	Propofol, Hippocampus volume, +8 days[71][72]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with propofol

Notes:

[71] - 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: Optional

[72] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.0 (± 0.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Thalamus volume, Baseline

End point title	Propofol, Thalamus volume, Baseline[73][74]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[73] - 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: Optional

[74] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.5 (± 1.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Thalamus volume, +4 hours

End point title	Propofol, Thalamus volume, +4 hours[75][76]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with propofol

Notes:

[75] - 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: Optional

[76] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.5 (± 1.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Thalamus volume, +1 day

End point title	Propofol, Thalamus volume, +1 day[77][78]

End point description:

End point type	Primary

End point timeframe:

+1 day after general anaesthesia with propofol

Notes:

[77] - 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: Optional

[78] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.8 (± 1.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Thalamus volume, +8 days

End point title	Propofol, Thalamus volume, +8 days[79][80]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with propofol

Notes:

[79] - 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: Optional

[80] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	15.5 (± 1.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Anterior Cingulate Cortex volume, Baseline

End point title	Propofol, Anterior Cingulate Cortex volume, Baseline[81][82]

End point description:

End point type	Primary

End point timeframe:

Baseline

Notes:

[81] - 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: Optional

[82] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.9 (± 1.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Anterior Cingulate Cortex volume, +4 hours

End point title	Propofol, Anterior Cingulate Cortex volume, +4 hours[83][84]

End point description:

End point type	Primary

End point timeframe:

+4 hours after emergence from general anaesthesia with propofol

Notes:

[83] - 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: Optional

[84] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.8 (± 1.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Anterior Cingulate Cortex volume, +1 day

End point title	Propofol, Anterior Cingulate Cortex volume, +1 day[85][86]

End point description:

End point type	Primary

End point timeframe:

+1 day after general anaesthesia with propofol

Notes:

[85] - 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: Optional

[86] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.8 (± 1.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Propofol, Anterior Cingulate Cortex volume, +8 days

End point title	Propofol, Anterior Cingulate Cortex volume, +8 days[87][88]

End point description:

End point type	Primary

End point timeframe:

+8 days after general anaesthesia with propofol

Notes:

[87] - 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: Optional

[88] - 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: Optional

End point values	Propofol			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: millilitre(s)				
arithmetic mean (standard deviation)	9.9 (± 1.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Eight days.	
Assessment type	Systematic

Dictionary used	
Dictionary name	None
Dictionary version	0

Reporting groups	
Reporting group title	All participants
Reporting group description: -	

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 23 (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 intervention consists of general anaesthesia will well-known medications that have been in use for decades for this purpose: sevoflurane and propofol. No adverse events were reported.

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? Yes

Date	Interruption	Restart date
12 March 2020	Due to COVID-19 restrictions and -related safety precautions, we had to temporarily close our trial.	20 August 2020
07 January 2021	Due to COVID-19 restrictions and -related safety precautions, we had to temporarily close our trial.	04 March 2021

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The trial was terminated after 21 instead of 30 participants for logistical reasons.
The following results are pending:
- Diffusion Tensor Imaging
- Resting state functional MRI
- Fatigue and wellbeing
- Cognitive performance

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32962743