



Clinical trial results:

Investigation of nociceptive and antinociceptive mechanisms under anesthesia using fMRI, EEG and noxious reflexes

Summary

EudraCT number	2009-016907-41
Trial protocol	DE
Global end of trial date	19 August 2013

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021
Summary attachment (see zip file)	Summary (Abstract-1.docx)

Trial information

Trial identification

Sponsor protocol code	fMRT-Nociception
-----------------------	------------------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Falk von Dincklage, Charité - Universitätsmedizin Berlin, +49 030450531227, falk.von-dincklage@charite.de
Scientific contact	Falk von Dincklage, Charité - Universitätsmedizin Berlin, +49 030450531227, falk.von-dincklage@charite.de

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2013
Global end of trial reached?	Yes
Global end of trial date	19 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of anaesthetics on the cerebral and spinal responsiveness to noxious stimulation

Protection of trial subjects:

General anesthesia was conducted according to clinical standards and appropriate guidelines. Protection by anesthetic standard monitoring and two anesthesiologists present of which at least one is a fully certified anesthesiology specialist.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	12
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects recruited via advertising at Charité - Universitätsmedizin Berlin

Pre-assignment

Screening details:

Screening was conducted by performing an awake measurement in der MRI-scanner to test whether the subjects were comfortable to stay there for at least 30mins and hold still to perform the measurements.

Period 1

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

Blinding implementation details:

No blinding in this study as it is an exploratory study.

Arms

Arm title	Main
-----------	------

Arm description:

All subjects in this arm

Arm type	All subjects of the trial
Investigational medicinal product name	Propofol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administration of Propofol as in clinical practice for general anesthesia according to hospital standards and appropriate guidelines (iv infusion at 0-10 µg/ml effect-side-concentrations)

Investigational medicinal product name	Remifentanil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administration of Remifentanil as in clinical practice for general anesthesia according to hospital standards and appropriate guidelines (iv infusion at 0-8 ng/ml effect-side-concentrations)

Number of subjects in period 1	Main
Started	12
Completed	12

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	12	12	
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)	12	12	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	6	6	

Subject analysis sets

Subject analysis set title	Full analysis
Subject analysis set type	Full analysis

Subject analysis set description:

Analysis of all subjects of which the recorded data could be analyzed.

Reporting group values	Full analysis		
Number of subjects	10		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	10		
From 65-84 years	0		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	5		
Male	5		

End points

End points reporting groups

Reporting group title	Main
Reporting group description: All subjects in this arm	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description: Analysis of all subjects of which the recorded data could be analyzed.	

Primary: Cerebral response evoked by nociceptive stimulus during deep anaesthesia

End point title	Cerebral response evoked by nociceptive stimulus during deep anaesthesia
End point description:	
End point type	Primary
End point timeframe: During deep anaesthesia of 10 µg/ml effect-site concentration of propofol	

End point values	Main	Full analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: microvolt*s				
arithmetic mean (standard error)	0.905 (± 0.173)	0.905 (± 0.173)		

Statistical analyses

Statistical analysis title	Cerebral effect nociceptive vs innocuous stimulus
Statistical analysis description: Statistical comparison whether the nociceptive stimulus evokes a cerebral response that differs from that evoked by the innocuous stimulus.	
Comparison groups	Main v Full analysis
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[1] - Exploratory analysis to investigate the effect of anesthetics on nociception

Secondary: Cerebral response evoked by innocuous stimulus during deep anaesthesia

End point title	Cerebral response evoked by innocuous stimulus during deep anaesthesia
-----------------	--

End point description:

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

End point timeframe:

During deep anaesthesia of 10 µg/ml effect-site concentration of propofol

End point values	Main	Full analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: microvolt*s				
arithmetic mean (standard error)	0.141 (± 0.052)	0.141 (± 0.052)		

Statistical analyses

Statistical analysis title	Cerebral effect nociceptive vs innocuous stimulus
-----------------------------------	---

Statistical analysis description:

Statistical comparison whether the nociceptive stimulus evokes a cerebral response that differs from that evoked by the innocuous stimulus.

Comparison groups	Main v Full analysis
-------------------	----------------------

Number of subjects included in analysis	20
---	----

Analysis specification	Pre-specified
------------------------	---------------

Analysis type	other ^[2]
---------------	----------------------

P-value	< 0.05
---------	--------

Method	t-test, 2-sided
--------	-----------------

Notes:

[2] - Exploratory analysis to investigate the effect of anesthetics on nociception

Secondary: Spinal response evoked by nociceptive stimulus during deep anaesthesia

End point title	Spinal response evoked by nociceptive stimulus during deep anaesthesia
-----------------	--

End point description:

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

End point timeframe:

During deep anaesthesia of 10 µg/ml effect-site concentration of propofol

End point values	Main	Full analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: microvolt*s				
arithmetic mean (standard error)	2.367 (± 0.505)	2.367 (± 0.505)		

Statistical analyses

Statistical analysis title	Spinal effect nociceptive vs innocuous stimulus
Statistical analysis description: Statistical comparison whether the nociceptive stimulus evokes a spinal response that differs from that evoked by the innocuous stimulus.	
Comparison groups	Main v Full analysis
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[3] - Exploratory analysis to investigate the effect of anesthetics on nociception

Secondary: Spinal response evoked by innocuous stimulus during deep anaesthesia

End point title	Spinal response evoked by innocuous stimulus during deep anaesthesia
End point description:	
End point type	Secondary
End point timeframe: During deep anaesthesia of 10 µg/ml effect-site concentration of propofol	

End point values	Main	Full analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: microvolt*s				
arithmetic mean (standard error)	0.024 (± 0.007)	0.024 (± 0.007)		

Statistical analyses

Statistical analysis title	Spinal effect nociceptive vs innocuous stimulus
Comparison groups	Main v Full analysis

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other ^[4]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[4] - Statistical comparison whether the nociceptive stimulus evokes a spinal response that differs from that evoked by the innocuous stimulus.

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Complete trial

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

Dictionary used

Dictionary name	SNOMED CT
-----------------	-----------

Dictionary version	2021-07-31
--------------------	------------

Reporting groups

Reporting group title	All trial participants
-----------------------	------------------------

Reporting group description:

All 12 subjects investigated in the trial

Serious adverse events	All trial participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All trial participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (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: As this exploratory study was conducted in only 12 healthy subjects and all medication was used only within normal clinical ranges, this trial did not have adverse events.

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/29935584>

<http://www.ncbi.nlm.nih.gov/pubmed/29421324>