



## Clinical trial results:

**Pilot-Study comparing analgosedation concepts during placement of regional anaesthesia with either fentanyl, remifentanyl, clonidine, EMLA-Patch or placebo in regard of patient's wellbeing, pain and satisfaction. A randomised, doubleblind, controlled pilot-study.**

### Summary

EudraCT number	2019-000700-14
Trial protocol	AT
Global end of trial date	18 October 2019

### Results information

Result version number	v1 (current)
This version publication date	23 December 2023
First version publication date	23 December 2023

### Trial information

#### Trial identification

Sponsor protocol code	2
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04026074
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Medical University of Graz
Sponsor organisation address	Neue Stiftingtalstraße 6, Graz, Austria, 8010
Public contact	Division of general anaesthesia, Medical University of Graz, gregor.schitteck@medunigraz.at
Scientific contact	Division of general anaesthesia, Medical University of Graz, gregor.schitteck@medunigraz.at

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 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 October 2019
Global end of trial reached?	Yes
Global end of trial date	18 October 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To specify the best analgosedation technic during placement of regional anaesthesia from the patients view (primary endpoint is pain intensity during placement of the regional anaesthesia).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice and regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 July 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	Austria: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	33
From 65 to 84 years	17
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted between July and October 2019.

### Pre-assignment

Screening details:

After informed consent 50 patients were randomized into one of five study arms.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Remifentanyl
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Arm description:

Remifentanyl infusion with a rate of 6 to 9 µg kg<sup>-1</sup> h<sup>-1</sup>

Arm type	Experimental
Investigational medicinal product name	remifentanyl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Remifentanyl infusion with a rate of 6 to 9 µg kg<sup>-1</sup> h<sup>-1</sup>

<b>Arm title</b>	Fentanyl
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Arm description:

intravenous bolus of 100 µg (body weight above 50 kg) or 50µg (body weight below 50 kg)

Arm type	Experimental
Investigational medicinal product name	Fentanyl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

intravenous bolus of 100 µg (body weight above 50 kg) or 50µg (body weight below 50 kg)

<b>Arm title</b>	Clonidine
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Arm description:

clonidine intravenous bolus of 150 µg

Arm type	Experimental
Investigational medicinal product name	Clonidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:  
clonidine intravenous bolus of 150 µg

<b>Arm title</b>	Lidocaine/Prilocaine
Arm description: Lidocaine/Prilocaine topical cream 1.5g/10cm <sup>2</sup>	
Arm type	Experimental
Investigational medicinal product name	Lidocaine/Prilocaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use

Dosage and administration details:

Lidocaine/Prilocaine topical cream 1.5g/10cm<sup>2</sup>; administered at least 30 minutes before skin puncture

<b>Arm title</b>	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion, Cream
Routes of administration	Cutaneous use, Intravenous use

Dosage and administration details:

Patients were administered i.v. placebo (0,9% NaCl) and placebo salve (skin protection salve)

<b>Number of subjects in period 1</b>	Remifentanil	Fentanyl	Clonidine
Started	9	12	9
Completed	9	12	9

<b>Number of subjects in period 1</b>	Lidocaine/Prilocaine	Placebo
Started	12	8
Completed	12	8

## Baseline characteristics

### Reporting groups

Reporting group title	Remifentanil
Reporting group description: Remifentanil infusion with a rate of 6 to 9 µg kg <sup>-1</sup> h <sup>-1</sup>	
Reporting group title	Fentanyl
Reporting group description: intravenous bolus of 100 µg (body weight above 50 kg) or 50µg (body weight below 50 kg)	
Reporting group title	Clonidine
Reporting group description: clonidine intravenous bolus of 150 µg	
Reporting group title	Lidocaine/Prilocaine
Reporting group description: Lidocaine/Prilocaine topical cream 1.5g/10cm <sup>2</sup>	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Remifentanil	Fentanyl	Clonidine
Number of subjects	9	12	9
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	58	61	47
standard deviation	± 19.8	± 18	± 21.6
Gender categorical Units: Subjects			
Female	5	7	6
Male	4	5	3

Reporting group values	Lidocaine/Prilocaine	Placebo	Total
Number of subjects	12	8	50
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days)			0 0 0

Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	55	60	
standard deviation	± 19.4	± 18	-
Gender categorical			
Units: Subjects			
Female	5	6	29
Male	7	2	21

## End points

### End points reporting groups

Reporting group title	Remifentanil
Reporting group description: Remifentanil infusion with a rate of 6 to 9 µg kg <sup>-1</sup> h <sup>-1</sup>	
Reporting group title	Fentanyl
Reporting group description: intravenous bolus of 100 µg (body weight above 50 kg) or 50µg (body weight below 50 kg)	
Reporting group title	Clonidine
Reporting group description: clonidine intravenous bolus of 150 µg	
Reporting group title	Lidocaine/Prilocaine
Reporting group description: Lidocaine/Prilocaine topical cream 1.5g/10cm <sup>2</sup>	
Reporting group title	Placebo
Reporting group description: -	

### Primary: Pain at puncture (categorised)

End point title	Pain at puncture (categorised)
End point description:	
End point type	Primary
End point timeframe: during placement of the regional anaesthesia	

End point values	Remifentanil	Fentanyl	Clonidine	Lidocaine/Prilocaine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	9	12
Units: Number of patients				
light pain (1 to 2)	7	5	1	6
medium or strong pain (from 3)	2	7	8	6

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Number of patients				
light pain (1 to 2)	3			
medium or strong pain (from 3)	5			

## Statistical analyses

<b>Statistical analysis title</b>	Pain at puncture (categorised)
Comparison groups	Remifentanyl v Fentanyl v Clonidine v Lidocaine/Prilocaine v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.08
Method	Chi-squared

## Primary: Pain at puncture

End point title	Pain at puncture
End point description:	
Numeric rating scale; 10 indicating the highest pain score	
End point type	Primary
End point timeframe:	
during placement of the regional anaesthesia	

<b>End point values</b>	Remifentanyl	Fentanyl	Clonidine	Lidocaine/Prilocaine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	9	12
Units: Units on numeric rating scale				
median (inter-quartile range (Q1-Q3))	2.00 (1.5 to 3.0)	3.00 (2.0 to 4.75)	4.0 (3.0 to 5.0)	2.5 (1.25 to 4.0)

<b>End point values</b>	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Units on numeric rating scale				
median (inter-quartile range (Q1-Q3))	3.00 (2.0 to 4.5)			

## Statistical analyses



<b>Statistical analysis title</b>	Pain at puncture
Comparison groups	Remifentanil v Fentanyl v Clonidine v Lidocaine/Prilocaine v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.172
Method	Kruskal-wallis

## Secondary: Complication rate

End point title	Complication rate
End point description:	
End point type	Secondary
End point timeframe:	
1 day	

<b>End point values</b>	Remifentanil	Fentanyl	Clonidine	Lidocaine/Prilocaine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	9	12
Units: Number of complications				
Number of complications	0	0	0	0

<b>End point values</b>	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Number of complications				
Number of complications	0			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Wellbeing

End point title	Wellbeing
End point description:	
Wellbeing assessment during placement of the regional anaesthesia was assessed with the anaesthesiological questionnaire (ANP).	
ANP is a self-rating method for the assessment of postoperative complaints, patient wellbeing and satisfaction. The rating scales from 0 to 3, with 0="none" and 3="strongly"). Higher wellbeing values represent a better outcome.	

End point type	Secondary
End point timeframe:	
1 day after surgery	

End point values	Remifentanil	Fentanyl	Clonidine	Lidocaine/Prilocaine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	12	9	12
Units: Number of patients				
None	0	0	0	1
Some	1	3	0	3
quite	6	8	9	7
Strong	2	0	0	1

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Number of patients				
None	0			
Some	1			
quite	6			
Strong	1			

### Statistical analyses

<b>Statistical analysis title</b>	Wellbeing
Comparison groups	Remifentanil v Fentanyl v Clonidine v Lidocaine/Prilocaine v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.535
Method	Chi-squared

## Adverse events

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

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Timeframe for reporting adverse events:  
from inclusion to end of study for the respective patient

Assessment type	Systematic
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### Dictionary used

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Dictionary name	MedDRA
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Dictionary version	23
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Frequency threshold for reporting non-serious adverse events: 5 %

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### 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 follow-up period per patient for this study was very short. No complications or adverse effects were observed during this time.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported