



Clinical trial results:

Requirement of Skeletal Muscle Paralysis in Hypothermic Patients after Cardiac Arrest. A pilot study

Summary

EudraCT number	2009-015771-27
Trial protocol	AT
Global end of trial date	12 December 2014

Results information

Result version number	v1 (current)
This version publication date	07 October 2020
First version publication date	07 October 2020
Summary attachment (see zip file)	Relax_Publication (Relax_Publication.pdf)

Trial information

Trial identification

Sponsor protocol code	V3
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01719770
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University Vienna, Emergency Medicine
Sponsor organisation address	Währinger Gürtel 18-20, Vienna, Austria, 1090 Wien
Public contact	Emergency Department, Medical University Vienna, Emergency Department, Medical University Vienna, +43 14040039530, heidrun.losert@meduniwien.ac.at
Scientific contact	Emergency Department, Medical University Vienna, Emergency Department, Medical University Vienna, +43 14040039530,

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	12 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2014
Global end of trial reached?	Yes
Global end of trial date	12 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Number of shivering episodes will be assessed and compared between the two groups with the Shivering Assessment Scale and the EMG.

Protection of trial subjects:

Intensive Care Patients were treated as usually, no painful or distressing examinations were done in these fully sedated, intubated patients.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2010
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: 63
Worldwide total number of subjects	63
EEA total number of subjects	63

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)	39
From 65 to 84 years	22
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

All patients with out of hospital cardiac arrest older than 18 years who presented to the emergency department with sustained return of spontaneous circulation who remained comatose.

Pre-assignment

Screening details:

Cardiac arrest had to be of presumed cardiopulmonary origin. Core body temperature had to be equal or above 35°C.

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, Data analyst, Subject, Assessor, Carer

Blinding implementation details:

A sealed envelope was opened by a nurse not involved in the treatment of the patient or the study. This person prepared the blinded anti-shivering bolus and continuous medication (neuromuscular blockers or saline)

Arms

Are arms mutually exclusive?	Yes
Arm title	Continuous-NMB-group

Arm description:

This group received a continuous rocuronium infusion and in case of shivering an saline bolus

Arm type	Experimental
Investigational medicinal product name	rocuronium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

0.25mg/kg/h

Arm title	Bolus-NMB-group
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Arm description:

Patients received saline infusion and in case of shivering a rocuronium bolus

Arm type	Active comparator
Investigational medicinal product name	rocuronium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.025ml/kg in case of shivering

Number of subjects in period 1	Continuous-NMB-group	Bolus-NMB-group
Started	32	31
Completed	32	31

Baseline characteristics

Reporting groups

Reporting group title	Continuous-NMB-group
Reporting group description:	
This group received a continuous rocuronium infusion and in case of shivering an saline bolus	
Reporting group title	Bolus-NMB-group
Reporting group description:	
Patients received saline infusion and in case of shivering a rocuronium bolus	

Reporting group values	Continuous-NMB-group	Bolus-NMB-group	Total
Number of subjects	32	31	63
Age categorical			
Only adults were included			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	19	38
From 65-84 years	11	12	23
85 years and over	2	0	2
Age continuous			
Only adult patients were included in the study			
Units: years			
arithmetic mean	62	58	
standard deviation	± 13	± 11	-
Gender categorical			
Units: Subjects			
Female	6	5	11
Male	26	26	52

End points

End points reporting groups

Reporting group title	Continuous-NMB-group
Reporting group description:	
This group received a continuous rocuronium infusion and in case of shivering an saline bolus	
Reporting group title	Bolus-NMB-group
Reporting group description:	
Patients received saline infusion and in case of shivering a rocuronium bolus	

Primary: subjects with shivering episodes

End point title	subjects with shivering episodes
End point description:	
Percentage of patients with shivering episodes	
End point type	Primary
End point timeframe:	
study period	

End point values	Continuous-NMB-group	Bolus-NMB-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: number of patients				
Percentage	8	29		

Statistical analyses

Statistical analysis title	primary analysis patients with shivering episodes
Comparison groups	Continuous-NMB-group v Bolus-NMB-group
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

Secondary: number of shivering episodes

End point title	number of shivering episodes
End point description:	
Median shivering episodes per group were reported	
End point type	Secondary

End point timeframe:
whole study period

End point values	Continuous-NMB-group	Bolus-NMB-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: median number of shivering episodes	0	8		

Statistical analyses

Statistical analysis title	number of shivering episodes
Comparison groups	Bolus-NMB-group v Continuous-NMB-group
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Doses of midazolam

End point title	Doses of midazolam
End point description:	
End point type	Secondary
End point timeframe: whole study period	

End point values	Continuous-NMB-group	Bolus-NMB-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: mg/kg				
geometric mean (standard deviation)	4.3 (± 0.8)	5.1 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Doses of fentanyl

End point title	Doses of fentanyl
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End point description:

End point type	Secondary
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End point timeframe:

whole study period

End point values	Continuous-NMB-group	Bolus-NMB-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: mg/kg				
geometric mean (standard deviation)	0.062 (\pm 0.014)	0.071 (\pm 0.007)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative doses of rocuronium

End point title	Cumulative doses of rocuronium
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End point description:

End point type	Secondary
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End point timeframe:

whole study period

End point values	Continuous-NMB-group	Bolus-NMB-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: mg/kg				
geometric mean (standard deviation)	7.8 (\pm 1.8)	2.3 (\pm 1.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall mortality

End point title	Overall mortality
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End point description:

End point type	Secondary
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End point timeframe:
whole study period

End point values	Continuous-NMB-group	Bolus-NMB-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: number of patients	15	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of favorable neurologic function after 12 months

End point title	Rate of favorable neurologic function after 12 months
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End point description:

End point type	Secondary
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End point timeframe:
whole study period

End point values	Continuous-NMB-group	Bolus-NMB-group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Number of patients	17	17		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

whole study period

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23
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Reporting groups

Reporting group title	Bolus Neuromuscular Blocker Group
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Reporting group description: -

Reporting group title	Continuous Neuromuscular Blocker Group
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Reporting group description: -

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: There were no non-serious adverse events

Serious adverse events	Bolus Neuromuscular Blocker Group	Continuous Neuromuscular Blocker Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 31 (3.23%)	1 / 32 (3.13%)	
number of deaths (all causes)	12	15	
number of deaths resulting from adverse events	0	0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax	Additional description: After out of hospital cardiopulmonary resuscitation a serial rib fracture caused a pneumothorax, which had to be treated with a drainage This is a common complication of cardiopulmonary reanimation and was not related with the study.		
subjects affected / exposed	1 / 31 (3.23%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematothorax	Additional description: Patient received routinely a central venous catheter - after 50 hours, a haematothorax after a mispunction of the left Artery subclavia appeared A thoracic Augean had to overstich the artery. This was not related to the study.		
subjects affected / exposed	0 / 31 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Bolus Neuromuscular Blocker Group	Continuous Neuromuscular Blocker Group	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 31 (0.00%)	0 / 32 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2010	The dosage of continuous rocuronium was adapted lower levels EMG will not be performed, only shivering assessment scale stress hormone levels will not be measured

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported