Clinical trial results:
The reversed isolated forearm technique to regionally reverse rocuronium induced muscle relaxation – a pilot study

Summary

EudraCT number	2013-002164-53
Trial protocol	AT
Global end of trial date	24 September 2015

Results information

Result version number	v1 (current)
This version publication date	27 March 2020
First version publication date	27 March 2020

Trial information

Trial identification

Sponsor protocol code	20130513

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria,
Public contact	Forschungsbüro, Fr. Mag. Vecs, Medizinische Universität Wien, Abteilung für Allgemeine Anästhesie und Intensivmedizin, +43 1404002031, eleonora.vecs@meduniwien.ac.at
Scientific contact	Forschungsbüro, Fr. Mag. Vecs, Medizinische Universität Wien, Abteilung für Allgemeine Anästhesie und Intensivmedizin, +43 1404002031, eleonora.vecs@meduniwien.ac.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	25 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 September 2015
Global end of trial reached?	Yes
Global end of trial date	24 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the feasibility of regionally reversing a rocuronium induced muscle relaxation and to determine the dose of sugammadex that is necessary to reach a train of four (TOF) ratio ≥ 0.9.

Protection of trial subjects:

Patients were closely observed intra- and postoperatively for any adverse reaction to the intervention.

Background therapy:

Elective surgery with the need of general anaesthesia and muscle relaxation with rocuronium.

Evidence for comparator:

No comparator

Actual start date of recruitment	09 December 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	Austria: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	20
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients unterging an elective operation with the need of general anaesthesia with muscle relaxation were asked preoperatively if they want to participate in the study.

Pre-assignment

Screening details:

Patients unterging an elective operation with the need of general anaesthesia with muscle relaxation were screened for eligibility preoperatively

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

none

Arms

Arm title	Baseline

Arm description:

Patients before proceeding to period "Dose finding" or "Dose effect"

Arm type	no intervention
Investigational medicinal product name	none
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Other use

Dosage and administration details:

no product was used at baseline

Number of subjects in period 1	Baseline
Started	20
Completed	20

Period 2

Period 2 title	Dose finding
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

none

Arms

Arm title	Dose finding

Arm description:

The dose-titration process was designed as follows. The ini- tial dose in the first patient was set to be sugammadex 0.5 mg kg−1 diluted in 30 ml normal saline. If the TOF ratio remained below 0.9 for the next 5 min, a top-up dose of one-quarter of this dose (e.g. sugammadex 0.125 mg kg−1 in Patient 1) diluted in 10 ml of 0.9% saline was administered. This procedure was re- peated until a stable TOF ratio ≥0.9 (three consecutive measure- ments ≥0.9) was reached in the interventional limb or until a total of four injections were given. If a TOF ratio ≥0.9 was achieved with this titration, the initial and top-up sugammadex doses in the next patient were reduced to one-quarter of the initial dose given to the previous patient but were still diluted in 30 ml saline (10 ml for top-up doses). For example, if the muscle paralysis of Patient 1 was antagonized after the initial dose of sugammadex 0.5 mg kg−1, the initial and the top-up doses would be reduced to 1.25 mg kg−1 in Patient 2.

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

Dosage and administration details:

The dose-titration process was designed as follows. The ini- tial dose in the first patient was set to be sugammadex 0.5 mg kg−1 diluted in 30 ml normal saline. If the TOF ratio remained below 0.9 for the next 5 min, a top-up dose of one-quarter of this dose (e.g. sugammadex 0.125 mg kg−1 in Patient 1) diluted in 10 ml of 0.9% saline was administered. This procedure was re- peated until a stable TOF ratio ≥0.9 (three consecutive measure- ments ≥0.9) was reached in the interventional limb or until a total of four injections were given. If a TOF ratio ≥0.9 was achieved with this titration, the initial and top-up sugammadex doses in the next patient were reduced to one-quarter of the initial dose given to the previous patient but were still diluted in 30 ml saline (10 ml for top-up doses). For example, if the muscle paralysis of Patient 1 was antagonized after the initial dose of sugammadex 0.5 mg kg−1, the initial and the top-up doses would be reduced to 1.25 mg kg−1 in Patient 2.

Number of subjects in period 2[1]	Dose finding
Started	10
Completed	10

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 20 Patients were included at baseline, 10 of these patients participated in study period "dose finding" and 10 of the patients participated in the period "time to effect". All patients completed the study

Period 3

Period 3 title	Dose effect
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

none

Arms

Arm title	Dose Effect

Arm description:

In this group, dose titration was not performed, and all patients received the same amount of sugammadex diluted in the same volume (30 ml normal saline). The TOF was again measured every 15 s in both arms, and the effects of the sugammadex dose on muscle paralysis in both arms were recorded. The tour- niquet was released 15 min after sugammadex was injected, and the effect of this dose on the TOF values in both arms was re- corded until the TOF ratio returned to ≥0.9 in both arms.

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

Dosage and administration details:

In this group, dose titration was not performed, and all patients received the same amount of sugammadex diluted in the same volume (30 ml normal saline). The TOF was again measured every 15 s in both arms, and the effects of the sugammadex dose on muscle paralysis in both arms were recorded. The tour- niquet was released 15 min after sugammadex was injected, and the effect of this dose on the TOF values in both arms was re- corded until the TOF ratio returned to ≥0.9 in both arms.

Number of subjects in period 3	Dose Effect
Started	10
Completed	10

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	20	20	
Age categorical			
Baseline characteristics			
Units: Subjects			
Adults (18-64 years)	20	20	
Age continuous			
Units: years			
arithmetic mean	38		
standard deviation	± 12	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	10	10	

Subject analysis sets	
Subject analysis set title	Dose finding of sugammadex
Subject analysis set type	Per protocol
Subject analysis set description: descriptive	
Subject analysis set title	Dose to effect
Subject analysis set type	Per protocol
Subject analysis set description: descriptive	

Reporting group values	Dose finding of sugammadex	Dose to effect	
Number of subjects	10	10	
Age categorical			
Baseline characteristics			
Units: Subjects			
Adults (18-64 years)	10	10	
Age continuous			
Units: years			
arithmetic mean	50	40	
standard deviation	± 11	± 14	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	5	5	

End points

End points reporting groups

Reporting group title	Baseline
Reporting group description:	
Patients before proceeding to period "Dose finding" or "Dose effect"	
Reporting group title	Dose finding
Reporting group description:	
The dose-titration process was designed as follows. The ini- tial dose in the first patient was set to be sugammadex 0.5 mg kg−1 diluted in 30 ml normal saline. If the TOF ratio remained below 0.9 for the next 5 min, a top-up dose of one-quarter of this dose (e.g. sugammadex 0.125 mg kg−1 in Patient 1) diluted in 10 ml of 0.9% saline was administered. This procedure was re- peated until a stable TOF ratio ≥0.9 (three consecutive measure- ments ≥0.9) was reached in the interventional limb or until a total of four injections were given. If a TOF ratio ≥0.9 was achieved with this titration, the initial and top-up sugammadex doses in the next patient were reduced to one-quarter of the initial dose given to the previous patient but were still diluted in 30 ml saline (10 ml for top-up doses). For example, if the muscle paralysis of Patient 1 was antagonized after the initial dose of sugammadex 0.5 mg kg−1, the initial and the top-up doses would be reduced to 1.25 mg kg−1 in Patient 2.	
Reporting group title	Dose Effect
Reporting group description:	
In this group, dose titration was not performed, and all patients received the same amount of sugammadex diluted in the same volume (30 ml normal saline). The TOF was again measured every 15 s in both arms, and the effects of the sugammadex dose on muscle paralysis in both arms were recorded. The tour- niquet was released 15 min after sugammadex was injected, and the effect of this dose on the TOF values in both arms was re- corded until the TOF ratio returned to ≥0.9 in both arms.	
Subject analysis set title	Dose finding of sugammadex
Subject analysis set type	Per protocol
Subject analysis set description:	
descriptive	
Subject analysis set title	Dose to effect
Subject analysis set type	Per protocol
Subject analysis set description:	
descriptive	

Primary: Dose of sugammadex

End point title	Dose of sugammadex
End point description:	
End point type	Primary
End point timeframe:	
5 minutes after the application of sugammadex	

End point values	Dose finding	Dose finding of sugammadex		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: mg/kg				
median (standard deviation)	0.02 (± 0.15)	0.02 (± 0.15)		

Statistical analyses

Statistical analysis title	descriptive
Statistical analysis description: Descriptive analysis	
Comparison groups	Dose finding v Dose finding of sugammadex
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.05 [2]
Method	descriptive statistics
Parameter estimate	descriptive statistics

Notes:
[1] - descriptive statistics
[2] - not applicable

Primary: Time to reversal of rocuronium

End point title	Time to reversal of rocuronium
End point description:	
End point type	Primary
End point timeframe: Time from the application of sugammadex to TOF >0.9	

End point values	Dose Effect	Dose to effect		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: minute				
arithmetic mean (standard deviation)	1.9 (± 1.3)	1.95 (± 1.35)		

Statistical analyses

Statistical analysis title	Time to effect
Comparison groups	Dose Effect v Dose to effect
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05 [3]
Method	descriptive statistics
Parameter estimate	descriptive statistics
Point estimate	0
Confidence interval	
level	Other: 0 %
sides	2-sided
lower limit	0
upper limit	0

Variability estimate	Standard deviation

Notes:

[3] - not applicable

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: at the day the study was performed	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15

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

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (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: In this small feasibility study, no adverse event was observed.

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/26934944