



Clinical trial results:

A single-blinded multicenter randomized interventional study of rocuronium 0.3 mg/kg, and 0.9 mg/kg comparing onset time, duration of action and effect on intubating conditions in elderly patients (80 years).

Summary

EudraCT number	2019-004343-76
Trial protocol	DK
Global end of trial date	21 May 2021

Results information

Result version number	v1 (current)
This version publication date	14 October 2021
First version publication date	14 October 2021

Trial information

Trial identification

Sponsor protocol code	NMBA_ELDERLY2019ROCU_DOSES
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04512313
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet
Sponsor organisation address	Inge Lehmanns Vej 6, Copenhagen, Denmark, DK-2100
Public contact	Department of Anaesthesia, Rigshospitalet, 45 35458043, lars.rasmussen.01@regionh.dk
Scientific contact	Department of Anaesthesia, Rigshospitalet, 61652212 35458043, lars.rasmussen.01@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	30 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2021
Global end of trial reached?	Yes
Global end of trial date	21 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to determine the onset time after rocuronium 0.3 mg/kg and 0.9 mg/kg in patients with age \geq 80 years.

Protection of trial subjects:

All subjects received anaesthesia and analgesia according to best practice and the Helsinki Declaration

Background therapy:

Propofol and fentanyl for induction of anaesthesia. Postoperative pain relief with multimodal analgesia

Evidence for comparator:

Previous studies have found longer onset of rocuronium in elderly if only 0.6 mg pr kg is used. We therefore wanted to test if tracheal intubation could be performed earlier with better conditions with a larger dose 0.9 mg/kg. This large dose would be expected to result in a very long duration of action so we decided to compare with a smaller dose of 0.3 mg/kg.

Actual start date of recruitment	17 December 2020
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: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

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)	0
From 65 to 84 years	23

85 years and over	14
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Subject disposition

Recruitment

Recruitment details:

A total of 37 elderly were recruited between 17 December 2020 and 21 May 2021 in Copenhagen, Denmark

Pre-assignment

Screening details:

We screened patients above 80 years of age scheduled for elective surgery with anticipated duration of more than one hour. Other inclusion criteria were ASA group I to III, total intravenous anaesthesia and use of tracheal intubation after rocuronium.

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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The allocation sequence was generated by a computer program (REDCap) and rocuronium was prepared by an investigator who drew up the drug in 10 ml syringes of equal volume. The attending anaesthetist, the patient, and the other investigators were blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Rocuronium 0.3 mg/kg

Arm description:

Rocuronium 0.3 mg/kg

Arm type	Active comparator
Investigational medicinal product name	Rocuronium
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Rocuronium 0.3 mg/kg was given after anaesthesia induction

Arm title	Rocuronium 0.9 mg/kg
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Arm description:

Rocuronium 0.9 mg/kg was given after anaesthesia induction

Arm type	Experimental
Investigational medicinal product name	Rocuronium
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Rocuronium 0.9 mg/kg was given after anaesthesia induction

Number of subjects in period 1	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg
Started	20	17
Completed	18	16
Not completed	2	1
Consent withdrawn by subject	1	-
Logistic	1	1

Baseline characteristics

Reporting groups

Reporting group title	Rocuronium 0.3 mg/kg
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Reporting group description:

Rocuronium 0.3 mg/kg

Reporting group title	Rocuronium 0.9 mg/kg
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Reporting group description:

Rocuronium 0.9 mg/kg was given after anaesthesia induction

Reporting group values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg	Total
Number of subjects	20	17	37
Age categorical			
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)	0	0	0
From 65-84 years	16	7	23
85 years and over	4	10	14
Age continuous			
Units: years			
arithmetic mean	83	85	
standard deviation	± 1.9	± 3.3	-
Gender categorical			
Units: Subjects			
Female	10	13	23
Male	10	4	14
ASA class			
ASA class			
Units: Subjects			
ASA II	9	10	19
ASA III	11	7	18

Subject analysis sets

Subject analysis set title	Intubated
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Subject analysis set type	Modified intention-to-treat
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Subject analysis set description:

Those intubated

Reporting group values	Intubated		
Number of subjects	34		
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)	0		
From 65-84 years	20		
85 years and over	14		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Gender categorical			
Units: Subjects			
Female			
Male			
ASA class			
ASA class			
Units: Subjects			
ASA II			
ASA III			

End points

End points reporting groups

Reporting group title	Rocuronium 0.3 mg/kg
Reporting group description:	
Rocuronium 0.3 mg/kg	
Reporting group title	Rocuronium 0.9 mg/kg
Reporting group description:	
Rocuronium 0.9 mg/kg was given after anaesthesia induction	
Subject analysis set title	Intubated
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Those intubated	

Primary: Onset time

End point title	Onset time
End point description:	
End point type	Primary
End point timeframe:	
From injection of rocuronium until TOF=0	

End point values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	16		
Units: seconds				
arithmetic mean (standard deviation)	227 (± 140)	108 (± 40)		

Statistical analyses

Statistical analysis title	onset time difference
Statistical analysis description:	
t-test	
Comparison groups	Rocuronium 0.3 mg/kg v Rocuronium 0.9 mg/kg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	119

Confidence interval	
level	95 %
sides	2-sided
lower limit	41
upper limit	196

Secondary: Duration of action

End point title	Duration of action
End point description:	
End point type	Secondary
End point timeframe:	
From rocuronium injection to TOF 0.9	

End point values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	11		
Units: Minutes				
arithmetic mean (standard deviation)	46 (± 13)	118 (± 43)		

Statistical analyses

Statistical analysis title	Duration of action
Comparison groups	Rocuronium 0.3 mg/kg v Rocuronium 0.9 mg/kg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	72
Confidence interval	
level	95 %
sides	2-sided
lower limit	49
upper limit	95

Secondary: IDS

End point title	IDS
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End point description:

End point type	Secondary
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End point timeframe:

At intubation

End point values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: score				
median (inter-quartile range (Q1-Q3))	2 (1 to 3)	1 (0 to 2)		

Statistical analyses

Statistical analysis title	IDS comparison
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Statistical analysis description:

Intubation difficulty score

Comparison groups	Rocuronium 0.3 mg/kg v Rocuronium 0.9 mg/kg
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18
Method	Wilcoxon (Mann-Whitney)

Secondary: Proportion with excellent intubation conditions

End point title	Proportion with excellent intubation conditions
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End point description:

Excellent intubation conditions according to Fuchs Buder

End point type	Secondary
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End point timeframe:

At intubation

End point values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg	Intubated	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	34	
Units: Numbers				
Yes	4	11	15	
No	14	5	19	

Statistical analyses

Statistical analysis title	Comparing proportions with excellent conditions
Comparison groups	Rocuronium 0.3 mg/kg v Rocuronium 0.9 mg/kg
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.77

Secondary: Use of videolaryngoscope

End point title	Use of videolaryngoscope
End point description:	
End point type	Secondary
End point timeframe:	
At intubation	

End point values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg	Intubated	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	16	34	
Units: Numbers				
Yes	8	6	14	
No	10	10	20	

Statistical analyses

Statistical analysis title	Comparing use of videolaryngoscope
Comparison groups	Rocuronium 0.3 mg/kg v Rocuronium 0.9 mg/kg

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.68
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.4

Secondary: Use of stylet

End point title	Use of stylet
End point description:	
End point type	Secondary
End point timeframe:	
At intubation	

End point values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: Numbers				
Yes	9	6		
No	9	10		

Statistical analyses

Statistical analysis title	Comparing use of stylet
Comparison groups	Rocuronium 0.3 mg/kg v Rocuronium 0.9 mg/kg
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.46

Secondary: IDS score above 0

End point title	IDS score above 0
End point description:	
End point type	Secondary
End point timeframe:	
At intubation	

End point values	Rocuronium 0.3 mg/kg	Rocuronium 0.9 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: Numbers				
Yes	4	6		
No	14	10		

Statistical analyses

Statistical analysis title	Comparing proportions with IDS>0
Comparison groups	Rocuronium 0.9 mg/kg v Rocuronium 0.3 mg/kg
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.45

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

7 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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Reporting groups

Reporting group title	Rocuronium 0.9 mg/kg
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Reporting group description: -

Reporting group title	Rocuronium 0.3 mg/kg
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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: We carefully examined potential adverse events according to the data on rocuronium

Serious adverse events	Rocuronium 0.9 mg/kg	Rocuronium 0.3 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Constipation	Additional description: Readmitted with constipation and hyponatremia		
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Rocuronium 0.9 mg/kg	Rocuronium 0.3 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	

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