# 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 |

**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 ≥ 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 |

## 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 anesthetist, 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 |

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 |
| 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 | |

| 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 |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| Those intubated | |

| **Reporting group values** | Intubated | | |
|---|---|---|---|
| Number of subjects | 34 | | |
| Age categorical<br>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<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | | |
| Gender categorical<br>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:<br>Rocuronium 0.3 mg/kg | |
| Reporting group title | Rocuronium 0.9 mg/kg |
| Reporting group description:<br>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:<br>Those intubated | |

| Primary: Onset time | |
|---|---|
| End point title | Onset time |
| End point description: | |
| End point type | Primary |
| End point timeframe:<br>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:<br>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 |

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: score | | | | |
| median (inter-quartile range (Q1-Q3)) | 2 (1 to 3) | 1 (0 to 2) | | |

**Statistical analyses**

| **Statistical analysis title** | IDS comparison |
|---|---|

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 |
|---|---|

End point description:
Excellent intubation conditions according to Fuchs Buder

| 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 | 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 |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22 |

| Reporting groups | |
|---|---|
| Reporting group title | Rocuronium 0.9 mg/kg |
| Reporting group description: - | |
| Reporting group title | Rocuronium 0.3 mg/kg |
| 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