Clinical trial results:
A Phase 4 Randomised, Active-Comparator Controlled Trial to Study the Efficacy and Safety of Sugammadex (MK-8616) for the Reversal of Neuromuscular Blockade Induced by Either Rocuronium Bromide or Vecuronium Bromide in Morbidly Obese Subjects

Summary

EudraCT number	2017-000188-33
Trial protocol	DK BE AT
Global end of trial date	29 January 2019

Results information

Result version number	v1 (current)
This version publication date	20 December 2019
First version publication date	20 December 2019

Trial information

Trial identification

Sponsor protocol code	MK-8616-146

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03346070
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

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 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this trial is to evaluate the safety and efficacy of Sugammadex when administered according to actual body weight (ABW) as compared to ideal body weight (IBW) for the reversal of both moderate and deep neuromuscular blockade (NMB) induced by either Rocuronium or Vecuronium in morbidly obese participants

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2018
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: 3
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Denmark: 10
Country: Number of subjects enrolled	Germany: 115
Country: Number of subjects enrolled	United States: 70
Worldwide total number of subjects	207
EEA total number of subjects	137

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)	1
Adults (18-64 years)	184
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Potential subjects were evaluated to determine if they fulfill entry requirements.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sugammadex 2 mg/kg Actual Body Weight (ABW)

Arm description:

Following administration of neuromuscular blocking agent (NMBA), participants received a single intravenous (i.v.) bolus of Sugammadex at 2 mg/kg as determined utilising participant ABW. A treatment dose of 2 mg/kg was used for reversal of moderate NMB.

Arm type	Experimental
Investigational medicinal product name	Sugammadex 2 mg/kg ABW
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Following administration of NMBA (Rocuronium or Vecuronium) to achieve moderate NMB, participants received a single i.v. bolus of Sugammadex (2 mg/kg by ABW) for reversal of moderate NMB.
Moderate NMB is defined as the reappearance of a second twitch (T2) in response to Train of Four (TOF) stimulations.

Investigational medicinal product name	Rocuronium or Vecuronium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

To achieve NMB, participants received steroidal NMBA Rocuronium Bromide or Vecuronium Bromide administered via i.v. infusion and dosed according to participant ABW. NMBAs were concomitant medications used per label as adjunct to general anesthesia.

Arm title	Sugammadex 2 mg/kg Ideal Body Weight (IBW)

Arm description:

Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 2 mg/kg as determined utilising participant IBW. A treatment dose of 2 mg/kg was used for reversal of moderate NMB.

Arm type	Experimental
Investigational medicinal product name	Sugammadex 2 mg/kg IBW
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Following administration of NMBA (Rocuronium or Vecuronium) to achieve moderate NMB, participants received a single i.v. bolus of Sugammadex (2 mg/kg by IBW) for reversal of moderate NMB.
Moderate NMB is defined as the reappearance of T2 in response to TOF stimulations.

Investigational medicinal product name	Rocuronium or Vecuronium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

To achieve NMB, participants received steroidal NMBA Rocuronium Bromide or Vecuronium Bromide administered via i.v. infusion and dosed according to participant ABW. NMBAs were concomitant medications used per label as adjunct to general anesthesia.

Arm title	Sugammadex 4 mg/kg ABW

Arm description:

Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant ABW. A treatment dose of 4 mg/kg was used for reversal of deep NMB.

Arm type	Experimental
Investigational medicinal product name	Sugammadex 4 mg/kg ABW
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Following administration of NMBA (Rocuronium or Vecuronium) to achieve deep NMB, participants received a single i.v. bolus of Sugammadex (4 mg/kg by ABW) for reversal of deep NMB.
Deep NMB is defined as no

response to TOF stimulations (TOF=0) and a detection target of 1-2 post-tetanic counts (PTCs).

Investigational medicinal product name	Rocuronium or Vecuronium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

To achieve NMB, participants received steroidal NMBA Rocuronium Bromide or Vecuronium Bromide administered via i.v. infusion and dosed according to participant ABW. NMBAs were concomitant medications used per label as adjunct to general anesthesia.

Arm title	Sugammadex 4 mg/kg IBW

Arm description:

Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant IBW. A treatment dose of 4 mg/kg was used for reversal of deep NMB.

Arm type	Experimental
Investigational medicinal product name	Sugammadex 4 mg/kg IBW
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Following administration of NMBA (Rocuronium or Vecuronium) to achieve deep NMB, participants received a single i.v. bolus of Sugammadex (4 mg/kg by IBW) for reversal of deep NMB.
Deep NMB is defined as no response to TOF stimulations (TOF=0) and a detection target of 1-2 post-tetanic counts (PTCs).

Investigational medicinal product name	Rocuronium or Vecuronium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

To achieve NMB, participants received steroidal NMBA Rocuronium Bromide or Vecuronium Bromide administered via i.v. infusion and dosed according to participant ABW. NMBAs were concomitant medications used per label as adjunct to general anesthesia.

Arm title	Neostigmine/Glycopyrrolate

Arm description:

Following administration of NMBA, participants received a single i.v. bolus containing both Neostigmine (50 µg/kg; up to 5 mg maximum dose) and Glycopyrrolate (10 µg/kg; up to 1 mg maximum dose) as determined utilising participant ABW. Neostigmine/Glycopyrrolate was used for reversal of moderate NMB. Active comparator treatment for reversal for deep NMB was not available.

Arm type	Active comparator
Investigational medicinal product name	Neostigmine + Glycopyrrolate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Following administration of NMBA (Rocuronium or Vecuronium) to achieve moderate NMB, participants received a single i.v. bolus of Neostigmine (50 µg/kg; 5 mg maximum) and Glycopyrrolate (10 µg/kg; 1 mg maximum), dosed according to participant ABW for reversal of moderate NMB. Moderate NMB is defined as the reappearance of T2 in response to TOF stimulations.

Investigational medicinal product name	Rocuronium or Vecuronium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

To achieve NMB, participants received steroidal NMBA Rocuronium Bromide or Vecuronium Bromide administered via i.v. infusion and dosed according to participant ABW. NMBAs were concomitant medications used per label as adjunct to general anesthesia.

Number of subjects in period 1	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW
Started	41	41	41
Treated	38	38	38
Completed	38	37	37
Not completed	3	4	4
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	-	-
Physician decision	-	-	-
Screen Failure	-	-	-

Study medication not received as planned	2	2	3
Lost to follow-up	-	2	1

Number of subjects in period 1	Sugammadex 4 mg/kg IBW	Neostigmine/Glycopyrrolate
Started	42	42
Treated	36	38
Completed	36	37
Not completed	6	5
Adverse event, serious fatal	-	1
Consent withdrawn by subject	1	-
Physician decision	1	1
Screen Failure	1	1
Study medication not received as planned	3	2
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Sugammadex 2 mg/kg Actual Body Weight (ABW)
Reporting group description:	
Following administration of neuromuscular blocking agent (NMBA), participants received a single intravenous (i.v.) bolus of Sugammadex at 2 mg/kg as determined utilising participant ABW. A treatment dose of 2 mg/kg was used for reversal of moderate NMB.	
Reporting group title	Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Reporting group description:	
Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 2 mg/kg as determined utilising participant IBW. A treatment dose of 2 mg/kg was used for reversal of moderate NMB.	
Reporting group title	Sugammadex 4 mg/kg ABW
Reporting group description:	
Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant ABW. A treatment dose of 4 mg/kg was used for reversal of deep NMB.	
Reporting group title	Sugammadex 4 mg/kg IBW
Reporting group description:	
Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant IBW. A treatment dose of 4 mg/kg was used for reversal of deep NMB.	
Reporting group title	Neostigmine/Glycopyrrolate
Reporting group description:	
Following administration of NMBA, participants received a single i.v. bolus containing both Neostigmine (50 µg/kg; up to 5 mg maximum dose) and Glycopyrrolate (10 µg/kg; up to 1 mg maximum dose) as determined utilising participant ABW. Neostigmine/Glycopyrrolate was used for reversal of moderate NMB. Active comparator treatment for reversal for deep NMB was not available.	

Reporting group values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW
Number of subjects	41	41	41
Age categorical			
As a result of the data convention used for calculation of age for this study, one subject is displayed in the "Adolescents [12-17 years]" reporting group. It was confirmed that this subject was 18 years of age at the time of signing informed consent and was eligible to be enrolled into the study.			
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	1	0
Adults (18-64 years)	36	35	39
From 65-84 years	5	5	2
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	47.7	47.6	46.4
standard deviation	± 14.4	± 14.5	± 11.2

Sex: Female, Male Units: Subjects			
Female	34	30	24
Male	7	11	17
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	4	2
White	39	37	39
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	4
Not Hispanic or Latino	38	40	37
Unknown or Not Reported	2	0	0

Reporting group values	Sugammadex 4 mg/kg IBW	Neostigmine/Glycopyrrolate	Total
Number of subjects	42	42	207
Age categorical			
As a result of the data convention used for calculation of age for this study, one subject is displayed in the "Adolescents [12-17 years]" reporting group. It was confirmed that this subject was 18 years of age at the time of signing informed consent and was eligible to be enrolled into the study.			
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	1
Adults (18-64 years)	37	37	184
From 65-84 years	5	5	22
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	49.2	47.7	
standard deviation	± 11.7	± 13.3	-
Sex: Female, Male Units: Subjects			
Female	32	29	149
Male	10	13	58
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	3	3	14

White	38	38	191
More than one race	0	1	1
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5	2	13
Not Hispanic or Latino	37	39	191
Unknown or Not Reported	0	1	3

End points

End points reporting groups

Reporting group title	Sugammadex 2 mg/kg Actual Body Weight (ABW)

Reporting group description:

Following administration of neuromuscular blocking agent (NMBA), participants received a single intravenous (i.v.) bolus of Sugammadex at 2 mg/kg as determined utilising participant ABW. A treatment dose of 2 mg/kg was used for reversal of moderate NMB.

Reporting group title	Sugammadex 2 mg/kg Ideal Body Weight (IBW)

Reporting group description:

Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 2 mg/kg as determined utilising participant IBW. A treatment dose of 2 mg/kg was used for reversal of moderate NMB.

Reporting group title	Sugammadex 4 mg/kg ABW

Reporting group description:

Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant ABW. A treatment dose of 4 mg/kg was used for reversal of deep NMB.

Reporting group title	Sugammadex 4 mg/kg IBW

Reporting group description:

Following administration of NMBA, participants received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant IBW. A treatment dose of 4 mg/kg was used for reversal of deep NMB.

Reporting group title	Neostigmine/Glycopyrrolate

Reporting group description:

Following administration of NMBA, participants received a single i.v. bolus containing both Neostigmine (50 µg/kg; up to 5 mg maximum dose) and Glycopyrrolate (10 µg/kg; up to 1 mg maximum dose) as determined utilising participant ABW. Neostigmine/Glycopyrrolate was used for reversal of moderate NMB. Active comparator treatment for reversal for deep NMB was not available.

Subject analysis set title	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Following administration of NMBA, participants
who received a single i.v. bolus of Sugammadex at 2 mg/kg as determined utilising participant ABW, and those who received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant ABW were pooled by dosing method across depth of NMB. Treatment doses of 2 mg/kg and 4 mg/kg were used for reversal of moderate NMB and deep NMB respectively.

Subject analysis set title	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Following administration of NMBA, participants
who received a single i.v. bolus of Sugammadex at 2 mg/kg as determined utilising participant IBW, and those who received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant IBW were pooled by dosing method across depth of NMB. Treatment doses of 2 mg/kg and 4 mg/kg were used for reversal of moderate NMB and deep NMB respectively.

Subject analysis set title	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Following administration of NMBA, participants
who received a single i.v. bolus of Sugammadex at 2 mg/kg as determined utilising participant ABW, and those who received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant ABW were pooled by dosing method across depth of NMB. Treatment doses of 2 mg/kg and 4 mg/kg were used for reversal of moderate NMB and deep NMB respectively.

Subject analysis set title	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Following administration of NMBA, participants

who received a single i.v. bolus of Sugammadex at 2 mg/kg as determined utilising participant IBW, and those who received a single i.v. bolus of Sugammadex at 4 mg/kg as determined utilising participant IBW were pooled by dosing method across depth of NMB. Treatment doses of 2 mg/kg and 4 mg/kg were used for reversal of moderate NMB and deep NMB respectively.

Primary: Time to Recovery (TTR) of Participant Train Of Four (TOF) Ratio to ≥0.9: Primary Kaplan-Meier Analysis

End point title	Time to Recovery (TTR) of Participant Train Of Four (TOF) Ratio to ≥0.9: Primary Kaplan-Meier Analysis

End point description:

The primary efficacy analysis of TTR of TOF ratio to ≥0.9 was performed by estimating event rates within each treatment group using the Kaplan-Meier method. TTR was monitored by applying electrical stimulations to the ulnar nerve every 15 seconds and assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to magnitudes of the first and fourth twitches respectively, after nerve stimulation. The T4/T1 ratio (TOF; expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB. A faster TTR of the TOF ratio to 0.9 indicates faster recovery from NMB. Analysis population consisted of all randomised participants dosed with both an NMBA and an NMB reversal agent (study treatment) with ≥1 post-randomisation efficacy assessment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Primary

End point timeframe:

Up to 76 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	37	36
Units: Minutes				
median (confidence interval 95%)	1.7 (1.5 to 2.1)	3.4 (2.2 to 4.4)	1.8 (1.5 to 2.1)	3.3 (2.4 to 4.2)

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	75	73	
Units: Minutes				
median (confidence interval 95%)	34.5 (27.0 to 67.4)	1.8 (1.6 to 2.1)	3.3 (2.6 to 4.1)	

Statistical analyses

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)

Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0075
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	3.1

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	25.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.72
upper limit	69.03

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	61.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.13
upper limit	266.77

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.44
upper limit	3.93

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	3.01

Primary: Percentage of Participants with Treatment-Emergent Sinus Bradycardia Events

End point title	Percentage of Participants with Treatment-Emergent Sinus Bradycardia Events

End point description:

The percentage of participants experiencing treatment-emergent bradycardia events were identified with continuous electrocardiogram (ECG) monitoring. Treatment-emergent sinus bradycardia is defined as a heart rate <60 bpm that has also decreased more than 20% compared to participant baseline heart rate value, sustained for at least 1 minute after administration of study intervention. Treatment-emergent sinus bradycardia events may or may not be considered an adverse event (AE), as determined by investigator judgment. Analysis population consisted of all randomised participants who received at least one dose of study treatment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Primary

End point timeframe:

Up to 35 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	38	36
Units: Percentage of participants				
number (not applicable)	5.3	2.6	5.3	5.6

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	76	74	
Units: Percentage of participants				
number (not applicable)	2.6	5.3	4.1	

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.602
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	15

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW

Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.969
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	13.5

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.567
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	15

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.571
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.8
upper limit	15

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.95
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.6
upper limit	10.9

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg IBW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.528
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.4
upper limit	15.9

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.709
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	9.6

Primary: Percentage of Participants with Treatment-Emergent Sinus Tachycardia Events

End point title	Percentage of Participants with Treatment-Emergent Sinus Tachycardia Events

End point description:

The percentage of participants experiencing treatment-emergent sinus tachycardia events were identified with continuous ECG monitoring. Treatment-emergent sinus tachycardia is defined as a heart rate ≥100 bpm that has also increased more than 20% compared to participant baseline heart rate value, sustained for at least 1 minute after administration of study intervention. Treatment-emergent sinus tachycardia events may or may not be considered an AE, as determined by investigator judgment. Analysis population consisted of all randomised participants who received at least one dose of study treatment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Primary

End point timeframe:

Up to 35 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	38	36
Units: Percentage of participants				
number (not applicable)	10.5	7.9	13.2	2.8

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	76	74	
Units: Percentage of participants				
number (not applicable)	7.9	11.8	5.4	

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.738
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	17.4

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.077
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	11.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	26.3

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.717
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	16.4

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.486
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	19.7

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.849
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.2
upper limit	12.4

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg IBW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.339
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	6.7

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.149
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	16.8

Primary: Percentage of Participants with Other Treatment-Emergent Cardiac Arrhythmia Events

End point title	Percentage of Participants with Other Treatment-Emergent Cardiac Arrhythmia Events

End point description:

The percentage of participants experiencing other treatment-emergent cardiac arrhythmia events were identified with continuous ECG monitoring. Other treatment-emergent cardiac arrhythmias are defined as new or worsening arrhythmias (e.g., atrial fibrillation, atrial tachyarrhythmia, ventricular fibrillation, or ventricular tachyarrhythmia), sustained for at least 1 minute after administration of study intervention. Worsening arrhythmia events may or may not be considered an AE, as determined by investigator judgment. Analysis population consisted of all randomised participants who received at least one dose of study treatment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Primary

End point timeframe:

Up to 35 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	38	36
Units: Percentage of participants				
number (not applicable)	0.0	2.6	0.0	0.0

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	76	74	
Units: Percentage of participants				
number (not applicable)	2.6	0.0	1.4	

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.299
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	6.7

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	9.4

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.326
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7
upper limit	7

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.335
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6
upper limit	7.1

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.935
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.1
upper limit	11.9

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg IBW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.326
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.8
upper limit	7.3

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.299
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	3.5

Primary: Percentage of Participants Experiencing an Adverse Event (AE) after Administration of Study Intervention

End point title	Percentage of Participants Experiencing an Adverse Event (AE) after Administration of Study Intervention

End point description:

The percentage of participants experiencing an AE following administration of study intervention was monitored. An AE is any unfavorable and unintended medical occurrence, symptom, or disease witnessed in a participant, regardless of whether or not a causal relationship with the study treatment can be demonstrated. Further, any worsening (i.e. any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition that is temporally associated with the use of the study treatment is also considered an AE. Analysis population consisted of all randomised participants who received at least one dose of study treatment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Primary

End point timeframe:

Up to 7 days

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	38	36
Units: Percentage of participants				
number (not applicable)	94.7	94.7	86.8	91.7

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	76	74	
Units: Percentage of participants				
number (not applicable)	89.5	90.8	93.2	

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.7
upper limit	13.1

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW

Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.6
upper limit	12.2

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	19.7

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18
upper limit	13.1

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.6
upper limit	19.2

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg IBW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	17

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.4
upper limit	7.8

Primary: Percentage of Participants Experiencing a Serious Adverse Event (SAE) after Administration of Study Intervention

End point title	Percentage of Participants Experiencing a Serious Adverse Event (SAE) after Administration of Study Intervention

End point description:

The percentage of participants experiencing an SAE following administration of study intervention was monitored. An SAE is an adverse event that: results in death; is life threatening; results in persistent or

significant disability or incapacity; results in or prolongs a hospitalization; is a congenital anomaly or birth defect; is a cancer; or may jeopardize the participant, potentially requiring medical or surgical intervention. Analysis population consisted of all randomised participants who received at least one dose of study treatment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Primary

End point timeframe:

Up to 7 days

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	38	36
Units: Percentage of participants				
number (not applicable)	2.6	5.3	0.0	8.3

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	76	74	
Units: Percentage of participants				
number (not applicable)	7.9	1.3	6.8	

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	9.1

Statistical analysis title	Difference in percentage of participants

Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.3
upper limit	1.3

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.8
upper limit	6.8

Statistical analysis title	Difference in percentage
Comparison groups	Sugammadex 4 mg/kg ABW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.2
upper limit	1.8

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17
upper limit	10.5

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg IBW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	15.5

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	1.2

Primary: Percentage of Participants Experiencing an Event of Clinical Interest (ECI) after Administration of Study Intervention

End point title	Percentage of Participants Experiencing an Event of Clinical Interest (ECI) after Administration of Study Intervention

End point description:

The percentage of participants experiencing an ECI following administration of study intervention was monitored. ECIs are a discrete set of both AEs and SAEs, specifically designated as such for the trial. For

the purposes of this investigation, ECIs included 1) drug-induced liver injury; 2) clinically-relevant arrhythmias, inclusive of bradycardia and tachycardia defined as events necessitating intervention, as determined by investigator judgment; and 3) instances of hypersensitivity and/or anaphylaxis adjudicated by an external expert Adjudication Committee. Analysis population consisted of all randomised participants who received at least one dose of study treatment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Primary

End point timeframe:

Up to 7 days

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	38	38	36
Units: Percentage of participants				
number (not applicable)	0.0	2.6	2.6	2.8

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	76	74	
Units: Percentage of participants				
number (not applicable)	2.6	1.3	2.7	

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	7.3

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	10.8

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.7
upper limit	7

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.2
upper limit	11.7

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	11

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg IBW v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	12

Secondary: Percentage of Participants with Prolonged (>10 minutes) Time to Recovery (TTR) of the Train Of Four (TOF) ratio to ≥0.9

End point title	Percentage of Participants with Prolonged (>10 minutes) Time to Recovery (TTR) of the Train Of Four (TOF) ratio to ≥0.9

End point description:

Following administration of study intervention, the percentage of participants experiencing prolonged (>10 minutes) recovery to a TOF ratio ≥0.9 was calculated. TTR was monitored by applying electrical stimulations to the ulnar nerve every 15 seconds and assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to magnitudes of the first and fourth twitches respectively, after nerve stimulation. The T4/T1 ratio (TOF; expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB. A faster TTR of the TOF ratio to 0.9 indicates faster recovery from NMB. Analysis population consisted of all randomised participants dosed with both an NMBA and an NMB reversal agent (study treatment) with ≥1 post-randomisation efficacy assessment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Secondary

End point timeframe:

Up to 76 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	37	36
Units: Percentage of participants				
number (not applicable)	7.9	5.4	2.7	0.0

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	75	73	
Units: Percentage of participants				
number (not applicable)	84.2	5.3	2.7	

Statistical analyses

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8
upper limit	16.9

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-76.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-87.2
upper limit	-57.6

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	-78.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-88.8
upper limit	-61.1

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	14.2

Statistical analysis title	Difference in percentage of participants
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage
Point estimate	2.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	11

Secondary: Time to Recovery (TTR) of Participant Train of Four (TOF) Ratio to ≥0.9: Secondary Geometric Mean Analysis

End point title	Time to Recovery (TTR) of Participant Train of Four (TOF) Ratio to ≥0.9: Secondary Geometric Mean Analysis

End point description:

The secondary efficacy analysis of TTR of participant TOF ratio to ≥0.9 was performed by estimating the geometric mean of TTR within each treatment group. TTR was monitored by applying electrical stimulations to the ulnar nerve every 15 seconds and assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to magnitudes of the first and fourth twitches respectively, after nerve stimulation. The T4/T1 ratio (TOF; expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB. A faster TTR of the TOF ratio to 0.9 indicates faster recovery from NMB. Analysis population consisted of all randomised participants dosed with both an NMBA and an NMB reversal agent (study treatment) with ≥1 post-randomisation efficacy assessment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Secondary

End point timeframe:

Up to 76 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	37	36
Units: Minutes				
geometric mean (confidence interval 95%)	2.0 (1.7 to 2.5)	3.2 (2.6 to 3.9)	1.9 (1.5 to 2.3)	3.5 (2.9 to 4.3)

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	75	73	
Units: Minutes				
geometric mean (confidence interval 95%)	23.1 (18.3 to 29.2)	2.0 (1.7 to 2.3)	3.3 (2.9 to 3.8)	

Statistical analyses

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	0.86

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.12

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.19

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.71

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	0.72

Secondary: Time to Recovery (TTR) of Participant Train of Four (TOF) Ratio to ≥0.8: Geometric Mean Analysis

End point title	Time to Recovery (TTR) of Participant Train of Four (TOF) Ratio to ≥0.8: Geometric Mean Analysis

End point description:

The efficacy analysis of TTR of participant TOF ratio to ≥0.8 was performed by estimating the geometric mean of TTR within each treatment group. TTR was monitored by applying electrical stimulations to the ulnar nerve every 15 seconds and assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to magnitudes of the first and fourth twitches respectively, after nerve stimulation. The T4/T1 ratio (TOF; expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB. A faster TTR of the TOF ratio to 0.8 indicates faster recovery from NMB. Analysis population consisted of all randomised participants dosed with both an NMBA and an NMB reversal agent (study treatment) with ≥1 post-randomisation efficacy assessment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Secondary

End point timeframe:

Up to 69 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	37	36
Units: Minutes				
geometric mean (confidence interval 95%)	1.6 (1.3 to 1.8)	2.5 (2.1 to 2.9)	1.5 (1.2 to 1.7)	2.6 (2.1 to 3.1)

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	75	73	
Units: Minutes				
geometric mean (confidence interval 95%)	16.6 (12.8 to 21.7)	1.5 (1.3 to 1.7)	2.5 (2.2 to 2.8)	

Statistical analyses

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.8

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.13

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.2

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.72

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.7

Secondary: Time to Recovery (TTR) of Participant Train of Four (TOF) Ratio to ≥0.7: Geometric Mean Analysis

End point title	Time to Recovery (TTR) of Participant Train of Four (TOF) Ratio to ≥0.7: Geometric Mean Analysis

End point description:

The efficacy analysis of TTR of participant TOF ratio to ≥0.7 was performed by estimating the geometric mean of TTR within each treatment group. TTR was monitored by applying electrical stimulations to the ulnar nerve every 15 seconds and assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to magnitudes of the first and fourth twitches respectively, after nerve stimulation. The T4/T1 ratio (TOF; expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB. A faster TTR of the TOF ratio to 0.7 indicates faster recovery from NMB. Analysis population consisted of all randomised participants dosed with both an NMBA and an NMB reversal agent (study treatment) with ≥1 post-randomisation efficacy assessment. As specified by the protocol, analysis was performed in treatment arms pooled by dosing method across depth of NMB as well as in all randomised treatment arms separated by depth of NMB.

End point type	Secondary

End point timeframe:

Up to 61 minutes

End point values	Sugammadex 2 mg/kg Actual Body Weight (ABW)	Sugammadex 2 mg/kg Ideal Body Weight (IBW)	Sugammadex 4 mg/kg ABW	Sugammadex 4 mg/kg IBW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	38	37	37	36
Units: Minutes				
geometric mean (confidence interval 95%)	1.4 (1.2 to 1.6)	2.1 (1.8 to 2.4)	1.3 (1.2 to 1.6)	2.0 (1.7 to 2.5)

End point values	Neostigmine/Glycopyrrolate	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW)	Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	38	75	73	
Units: Minutes				
geometric mean (confidence interval 95%)	10.9 (8.1 to 14.6)	1.4 (1.2 to 1.5)	2.1 (1.8 to 2.3)	

Statistical analyses

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Sugammadex 2 mg/kg Ideal Body Weight (IBW)
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.81

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Actual Body Weight (ABW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.17

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 2 mg/kg Ideal Body Weight (IBW) v Neostigmine/Glycopyrrolate
Number of subjects included in analysis	75
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	0.27

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex 4 mg/kg ABW v Sugammadex 4 mg/kg IBW

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.83

Statistical analysis title	Difference in time to recovery
Comparison groups	Sugammadex ABW (2 mg/kg ABW plus 4 mg/kg ABW) v Sugammadex IBW (2 mg/kg IBW plus 4 mg/kg IBW)
Number of subjects included in analysis	148
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Ratio of geometric means
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.77

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 14 days	
Adverse event reporting additional description:	
Analysis population consisted of all randomised participants who received at least one dose of study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Sugammadex 2 mg/kg ABW
Reporting group description: -	
Reporting group title	Sugammadex 2 mg/kg IBW
Reporting group description: -	
Reporting group title	Sugammadex 4 mg/kg ABW
Reporting group description: -	
Reporting group title	Sugammadex 4 mg/kg IBW
Reporting group description: -	
Reporting group title	Neostigmine + Glycopyrrolate
Reporting group description: -	

Serious adverse events	Sugammadex 2 mg/kg ABW	Sugammadex 2 mg/kg IBW	Sugammadex 4 mg/kg ABW
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 38 (2.63%)	3 / 38 (7.89%)	0 / 38 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Borderline ovarian tumour			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Postoperative wound complication			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Myocardial infarction			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular Insufficiency			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Sugammadex 4 mg/kg IBW	Neostigmine + Glycopyrrolate	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 36 (11.11%)	3 / 38 (7.89%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Borderline ovarian tumour			
subjects affected / exposed	1 / 36 (2.78%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Postoperative wound complication			
subjects affected / exposed	1 / 36 (2.78%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 36 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tachyarrhythmia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular Insufficiency			

subjects affected / exposed	0 / 36 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	1 / 36 (2.78%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 36 (0.00%)	1 / 38 (2.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 38 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Sugammadex 2 mg/kg ABW	Sugammadex 2 mg/kg IBW	Sugammadex 4 mg/kg ABW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 38 (94.74%)	36 / 38 (94.74%)	32 / 38 (84.21%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	3 / 38 (7.89%)
occurrences (all)	1	2	3
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	1 / 38 (2.63%)
occurrences (all)	1	2	1
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	1 / 38 (2.63%)
occurrences (all)	0	2	1
Heart rate increased			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Oxygen saturation decreased			
subjects affected / exposed	0 / 38 (0.00%)	2 / 38 (5.26%)	1 / 38 (2.63%)
occurrences (all)	0	2	1
Injury, poisoning and procedural			

complications			
Anaemia postoperative			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences (all)	0	0	1
Incision site pain			
subjects affected / exposed	6 / 38 (15.79%)	4 / 38 (10.53%)	1 / 38 (2.63%)
occurrences (all)	6	4	1
Neuromuscular block prolonged			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	9 / 38 (23.68%)	4 / 38 (10.53%)	8 / 38 (21.05%)
occurrences (all)	10	4	8
Procedural pain			
subjects affected / exposed	28 / 38 (73.68%)	28 / 38 (73.68%)	23 / 38 (60.53%)
occurrences (all)	30	31	23
Procedural vomiting			
subjects affected / exposed	2 / 38 (5.26%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	3	2	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	1	1	1
Cardiovascular disorder			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	2 / 38 (5.26%)
occurrences (all)	0	1	2
Sinus tachycardia			
subjects affected / exposed	1 / 38 (2.63%)	3 / 38 (7.89%)	0 / 38 (0.00%)
occurrences (all)	1	3	0
Tachycardia			
subjects affected / exposed	2 / 38 (5.26%)	3 / 38 (7.89%)	4 / 38 (10.53%)
occurrences (all)	2	3	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	3 / 38 (7.89%)
occurrences (all)	1	1	3
Headache			

subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 38 (5.26%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	2	2	0
Leukocytosis			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 38 (10.53%)	5 / 38 (13.16%)	1 / 38 (2.63%)
occurrences (all)	4	5	1
Diarrhoea			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	1	2	0
Nausea			
subjects affected / exposed	6 / 38 (15.79%)	10 / 38 (26.32%)	9 / 38 (23.68%)
occurrences (all)	6	13	10
Short-bowel syndrome			
subjects affected / exposed	1 / 38 (2.63%)	3 / 38 (7.89%)	1 / 38 (2.63%)
occurrences (all)	1	3	1
Vomiting			
subjects affected / exposed	0 / 38 (0.00%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 38 (0.00%)	0 / 38 (0.00%)	2 / 38 (5.26%)
occurrences (all)	0	0	2
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 38 (2.63%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	1	2	1
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	2 / 38 (5.26%)	5 / 38 (13.16%)	2 / 38 (5.26%)
occurrences (all)	2	5	2
Hypokalaemia			
subjects affected / exposed	1 / 38 (2.63%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 38 (2.63%)	2 / 38 (5.26%)	0 / 38 (0.00%)
occurrences (all)	1	2	0
Metabolic acidosis			
subjects affected / exposed	2 / 38 (5.26%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences (all)	2	0	0

Non-serious adverse events	Sugammadex 4 mg/kg IBW	Neostigmine + Glycopyrrolate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 36 (88.89%)	32 / 38 (84.21%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 36 (5.56%)	3 / 38 (7.89%)	
occurrences (all)	2	4	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 36 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Pyrexia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 36 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	2 / 36 (5.56%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			

Insomnia			
subjects affected / exposed	2 / 36 (5.56%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 38 (0.00%)	
occurrences (all)	1	0	
Heart rate increased			
subjects affected / exposed	0 / 36 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	3	
Oxygen saturation decreased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	2 / 36 (5.56%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Incision site pain			
subjects affected / exposed	2 / 36 (5.56%)	3 / 38 (7.89%)	
occurrences (all)	2	3	
Neuromuscular block prolonged			
subjects affected / exposed	0 / 36 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Procedural nausea			
subjects affected / exposed	4 / 36 (11.11%)	5 / 38 (13.16%)	
occurrences (all)	4	5	
Procedural pain			
subjects affected / exposed	27 / 36 (75.00%)	24 / 38 (63.16%)	
occurrences (all)	27	25	
Procedural vomiting			
subjects affected / exposed	0 / 36 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	3 / 36 (8.33%)	1 / 38 (2.63%)	
occurrences (all)	3	1	

Cardiovascular disorder			
subjects affected / exposed	1 / 36 (2.78%)	1 / 38 (2.63%)	
occurrences (all)	1	1	
Sinus tachycardia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 38 (2.63%)	
occurrences (all)	1	1	
Tachycardia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 36 (2.78%)	1 / 38 (2.63%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	2 / 36 (5.56%)	1 / 38 (2.63%)	
occurrences (all)	2	2	
Syncope			
subjects affected / exposed	2 / 36 (5.56%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 36 (5.56%)	1 / 38 (2.63%)	
occurrences (all)	2	1	
Leukocytosis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	4 / 36 (11.11%)	2 / 38 (5.26%)	
occurrences (all)	4	2	
Diarrhoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 38 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	6 / 36 (16.67%)	7 / 38 (18.42%)	
occurrences (all)	6	7	
Short-bowel syndrome			

subjects affected / exposed	0 / 36 (0.00%)	1 / 38 (2.63%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	2 / 36 (5.56%)	0 / 38 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 38 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 36 (0.00%)	3 / 38 (7.89%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 36 (2.78%)	2 / 38 (5.26%)	
occurrences (all)	1	2	
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 38 (5.26%)	
occurrences (all)	0	2	
Hypomagnesaemia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 38 (2.63%)	
occurrences (all)	1	1	
Metabolic acidosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 38 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 August 2018	Primary reason for amendment was to incorporate revisions to the trial flow chart to provide flexibility to trial sites.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 August 2018	There was a brief stoppage of enrollment in the EU (Austria, Belgium, Denmark, and Germany) due to a recall of glycopyrronium bromide. The recall was initiated as a precaution due to the risk of capillary cracks of the ampules. The sponsor initiated Clinical Stock Recovery Action at EU investigative sites which included halting enrollment. Glycopyrronium bromide originally distributed was retrieved and new glycopyrronium bromide was sourced and distributed, upon which enrollment resumed.	07 November 2018

Notes:

Limitations and caveats

None reported