Clinical trial results:
A Phase 4 Double-Blinded, Randomized, Active Comparator-Controlled Clinical Trial to Study the Efficacy, Safety, and Pharmacokinetics of Sugammadex (MK-8616) for Reversal of Neuromuscular Blockade in Pediatric Participants

Summary

EudraCT number	2017-000692-92
Trial protocol	AT ES FI BE DK
Global end of trial date	28 January 2020

Results information

Result version number	v1
This version publication date	09 August 2020
First version publication date	09 August 2020

Trial information

Trial identification

Sponsor protocol code	8616-089

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03351608
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2020
Global end of trial reached?	Yes
Global end of trial date	28 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This trial will evaluate the safety and pharmacokinetics (PK) of sugammadex for the reversal of both moderate and deep neuromuscular blockade (NMB) induced by either rocuronium (ROC) or vecuronium (VEC) in pediatric participants. The primary efficacy hypothesis of this investigation is that sugammadex is superior to neostigmine in reversing moderate NMB in pediatric participants as measured by time to recovery to a train-of-four (TOF) ratio of ≥0.9.

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	12 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 26
Country: Number of subjects enrolled	Belgium: 27
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	Finland: 24
Country: Number of subjects enrolled	Germany: 67
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	Turkey: 16
Country: Number of subjects enrolled	United States: 93
Worldwide total number of subjects	288
EEA total number of subjects	179

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)	214
Adolescents (12-17 years)	74
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male and female participants 2 to <17 years of age who are categorized as American Society of Anesthesiologists (ASA) Physical Class 1, 2, or 3 and had a planned medical and/or surgical procedure requiring moderate or deep NMB with ROC or VEC that would allow for neuromuscular monitoring were recruited.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Sugammadex 2 mg/kg

Arm description:

For moderate NMB reversal, a single intravenous (i.v.) bolus of sugammadex (2 mg/kg) was given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.

Arm type	Experimental
Investigational medicinal product name	Sugammadex
Investigational medicinal product code	
Other name	MK-8616 BRIDION
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For moderate NMB reversal, a single i.v. bolus of sugammadex (2 mg/kg) is given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.

Arm title	Part A: Sugammadex 4 mg

Arm description:

For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).

Arm type	Experimental
Investigational medicinal product name	Sugammadex
Investigational medicinal product code	
Other name	MK-8616 BRIDION
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) is given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).

Arm title	Part B: Sugammadex 2 mg/kg

Arm description:

For moderate NMB reversal, a single i.v. bolus of sugammadex (2 mg/kg) was given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the

reappearance of a second twitch (T2) in response to TOF stimulations.

Arm type	Experimental
Investigational medicinal product name	Sugammadex
Investigational medicinal product code	
Other name	MK-8616 BRIDION
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For moderate NMB reversal, a single i.v. bolus of sugammadex (2 mg/kg) is given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.

Arm title	Part B: Sugammadex 4 mg/kg

Arm description:

For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).

Arm type	Experimental
Investigational medicinal product name	Sugammadex
Investigational medicinal product code	
Other name	MK-8616 BRIDION
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) is given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).

Arm title	Part B: Neostigmine + (Glycopyrrolate or Atropine)

Arm description:

For moderate NMB reversal, a single i.v. bolus containing both neostigmine (50 µg/kg; up to 5 mg maximum dose) as well as either glycopyrrolate (10 µg/kg) or atropine (20 µg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.

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

Dosage and administration details:

For moderate NMB reversal, a single i.v. bolus containing both neostigmine (50 µg/kg; up to 5 mg maximum dose) as well as atropine (20 µg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.

Investigational medicinal product name	Neostigmine + Glycopyrrolate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

For moderate NMB reversal, a single i.v. bolus containing both neostigmine (50 µg/kg; up to 5 mg maximum dose) as well as glycopyrrolate (10 µg/kg) will be given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.

Number of subjects in period 1	Part A: Sugammadex 2 mg/kg	Part A: Sugammadex 4 mg	Part B: Sugammadex 2 mg/kg
Started	19	23	35
Completed	18	21	32
Not completed	1	2	3
Randomized by mistake, no treatment given	-	-	-
Physician decision	1	-	-
Other	-	1	1
Lost to follow-up	-	1	1
Withdrawal by parent/guardian	-	-	1

Number of subjects in period 1	Part B: Sugammadex 4 mg/kg	Part B: Neostigmine + (Glycopyrrolate or Atropine)
Started	176	35
Completed	168	33
Not completed	8	2
Randomized by mistake, no treatment given	1	-
Physician decision	2	1
Other	3	-
Lost to follow-up	1	1
Withdrawal by parent/guardian	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Sugammadex 2 mg/kg
Reporting group description:	
For moderate NMB reversal, a single intravenous (i.v.) bolus of sugammadex (2 mg/kg) was given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.	
Reporting group title	Part A: Sugammadex 4 mg
Reporting group description:	
For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).	
Reporting group title	Part B: Sugammadex 2 mg/kg
Reporting group description:	
For moderate NMB reversal, a single i.v. bolus of sugammadex (2 mg/kg) was given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.	
Reporting group title	Part B: Sugammadex 4 mg/kg
Reporting group description:	
For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).	
Reporting group title	Part B: Neostigmine + (Glycopyrrolate or Atropine)
Reporting group description:	
For moderate NMB reversal, a single i.v. bolus containing both neostigmine (50 µg/kg; up to 5 mg maximum dose) as well as either glycopyrrolate (10 µg/kg) or atropine (20 µg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.	

Reporting group values	Part A: Sugammadex 2 mg/kg	Part A: Sugammadex 4 mg	Part B: Sugammadex 2 mg/kg
Number of subjects	19	23	35
Age Categorical Units: Subjects			
Children (2-11 years)	15	17	25
Adolescents (12-17 years)	4	6	10
Age Continuous Units: years			
arithmetic mean	7.1	7.2	7.9
standard deviation	± 4.7	± 5.0	± 4.4
Gender Categorical Units: Subjects			
Female	11	12	20
Male	8	11	15
Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	0	2	3
Black or African American	1	2	1
Multiple	2	1	0
White	16	17	30

Not Reported	0	0	1

Reporting group values	Part B: Sugammadex 4 mg/kg	Part B: Neostigmine + (Glycopyrrolate or Atropine)	Total
Number of subjects	176	35	288
Age Categorical Units: Subjects			
Children (2-11 years)	132	25	214
Adolescents (12-17 years)	44	10	74
Age Continuous Units: years			
arithmetic mean	7.9	8.7	
standard deviation	± 4.4	± 4.4	-
Gender Categorical Units: Subjects			
Female	95	18	156
Male	81	17	132
Race Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	5	2	12
Black or African American	2	0	6
Multiple	4	0	7
White	161	33	257
Not Reported	4	0	5

End points

End points reporting groups

Reporting group title	Part A: Sugammadex 2 mg/kg
Reporting group description:	
For moderate NMB reversal, a single intravenous (i.v.) bolus of sugammadex (2 mg/kg) was given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.	
Reporting group title	Part A: Sugammadex 4 mg
Reporting group description:	
For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).	
Reporting group title	Part B: Sugammadex 2 mg/kg
Reporting group description:	
For moderate NMB reversal, a single i.v. bolus of sugammadex (2 mg/kg) was given after final dose of neuromuscular blocking agent (NMBA; rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.	
Reporting group title	Part B: Sugammadex 4 mg/kg
Reporting group description:	
For deep NMB reversal, a single i.v. bolus of sugammadex (4 mg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of detection of a target of 1 to 2 post-tetanic counts and no response to TOF stimulations (TOF=0).	
Reporting group title	Part B: Neostigmine + (Glycopyrrolate or Atropine)
Reporting group description:	
For moderate NMB reversal, a single i.v. bolus containing both neostigmine (50 µg/kg; up to 5 mg maximum dose) as well as either glycopyrrolate (10 µg/kg) or atropine (20 µg/kg) was given after final dose of NMBA (rocuronium or vecuronium) and within 2 minutes of the reappearance of a second twitch (T2) in response to TOF stimulations.	
Subject analysis set title	Part A: Sugammadex 2 mg (2 to <6 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Part A receiving sugammadex 2 mg and who are 2 to <6 years of age are included.	
Subject analysis set title	Part A: Sugammadex 2 mg (6 to <12 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Part A receiving sugammadex 2 mg and who are 6 to <12 years of age are included.	
Subject analysis set title	Part A: Sugammadex 2 mg (12 to <17 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Part A receiving sugammadex 2 mg and who are 12 to <17 years of age are included.	
Subject analysis set title	Part A: Sugammadex 4 mg (2 to <6 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Part A receiving sugammadex 4 mg and who are 2 to <6 years of age are included.	
Subject analysis set title	Part A: Sugammadex 4 mg (6 to <12 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Part A receiving sugammadex 4 mg and who are 6 to <12 years of age are included.	
Subject analysis set title	Part A: Sugammadex 4 mg (12 to <17 years)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Part A receiving sugammadex 4 mg and who are 12 to <17 years of age are included.	
Subject analysis set title	Parts A and B: Sugammadex 2 mg

Subject analysis set type	Safety analysis

Subject analysis set description:

All participants in Parts A and B who received sugammadex 2 mg are included in the analysis.

Subject analysis set title	Parts A and B: Sugammadex 4 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

All participants in Parts A and B who received sugammadex 4 mg are included in the analysis.

Primary: Area Under the Plasma Concentration-Time Curve (AUC) from Dosing to Infinity (AUC0-∞) of Sugammadex [Part A]

End point title	Area Under the Plasma Concentration-Time Curve (AUC) from Dosing to Infinity (AUC0-∞) of Sugammadex [Part A][1]

End point description:

The AUCo-∞ for sugammadex, defined as the area under the plasma concentration versus time plot, was
determined in each Part A arm. All participants with ≥5 post-dosing samples available are included.

End point type	Primary

End point timeframe:

2 minutes (min), 15 min, 30 min, 60 min, 4-6 hours (hrs), and 10 hrs post-dose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part A: Sugammadex 2 mg (2 to <6 years)	Part A: Sugammadex 2 mg (6 to <12 years)	Part A: Sugammadex 2 mg (12 to <17 years)	Part A: Sugammadex 4 mg (2 to <6 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	4	8
Units: hr*µg/mL				
geometric mean (geometric coefficient of variation)	14.1 (± 19.4)	18.8 (± 27.4)	27.6 (± 58.0)	26.9 (± 18.5)

End point values	Part A: Sugammadex 4 mg (6 to <12 years)	Part A: Sugammadex 4 mg (12 to <17 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: hr*µg/mL				
geometric mean (geometric coefficient of variation)	38.2 (± 73.0)	49.2 (± 20.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Clearance (CL) of Sugammadex [Part A]

End point title	Plasma Clearance (CL) of Sugammadex [Part A][2]

End point description:

The CL of sugammadex, defined as the rate of elimination relative to plasma concentration, was determined in each Part A arm. All participants with ≥5 post-dosing samples available are included.

End point type	Primary

End point timeframe:

2 minutes (min), 15 min, 30 min, 60 min, 4-6 hours (hrs), and 10 hrs post-dose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part A: Sugammadex 2 mg (2 to <6 years)	Part A: Sugammadex 2 mg (6 to <12 years)	Part A: Sugammadex 2 mg (12 to <17 years)	Part A: Sugammadex 4 mg (2 to <6 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	4	8
Units: L/hr				
geometric mean (geometric coefficient of variation)	2.30 (± 21.4)	3.58 (± 26.2)	4.68 (± 52.5)	2.26 (± 29.4)

End point values	Part A: Sugammadex 4 mg (6 to <12 years)	Part A: Sugammadex 4 mg (12 to <17 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: L/hr				
geometric mean (geometric coefficient of variation)	3.43 (± 105)	5.69 (± 24.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (Vz) of Sugammadex [Part A]

End point title	Apparent Volume of Distribution (Vz) of Sugammadex [Part

End point description:

The Vz of sugammadex, defined as the amount of drug administered relative to plasma concentrations, was determined in each Part A arm. All participants with ≥5 post-dosing samples available are included.

End point type	Primary

End point timeframe:

2 minutes (min), 15 min, 30 min, 60 min, 4-6 hours (hrs), and 10 hrs post-dose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part A: Sugammadex 2 mg (2 to <6 years)	Part A: Sugammadex 2 mg (6 to <12 years)	Part A: Sugammadex 2 mg (12 to <17 years)	Part A: Sugammadex 4 mg (2 to <6 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	4	8
Units: Liters				
geometric mean (geometric coefficient of variation)	3.58 (± 21.3)	6.65 (± 33.5)	10.8 (± 34.8)	4.00 (± 37.7)

End point values	Part A: Sugammadex 4 mg (6 to <12 years)	Part A: Sugammadex 4 mg (12 to <17 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: Liters				
geometric mean (geometric coefficient of variation)	8.22 (± 82.9)	12.3 (± 35.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Plasma Concentration (Cmax) of Sugammadex [Part A]

End point title	Maximum Plasma Concentration (Cmax) of Sugammadex [Part A][4]

End point description:

The Cmax of sugammadex, defined as the maximum plasma concentration, was determined in each Part A arm. All
participants with ≥5 post-dosing samples available are included.

End point type	Primary

End point timeframe:

2 minutes (min), 15 min, 30 min, 60 min, 4-6 hours (hrs), and 10 hrs post-dose

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part A: Sugammadex 2 mg (2 to <6 years)	Part A: Sugammadex 2 mg (6 to <12 years)	Part A: Sugammadex 2 mg (12 to <17 years)	Part A: Sugammadex 4 mg (2 to <6 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	4	8
Units: µg/mL				
geometric mean (geometric coefficient of variation)	17.5 (± 33.1)	32.2 (± 15.6)	41.3 (± 85.8)	47.1 (± 22.1)

End point values	Part A: Sugammadex 4 mg (6 to <12 years)	Part A: Sugammadex 4 mg (12 to <17 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: µg/mL				
geometric mean (geometric coefficient of variation)	51.6 (± 69.2)	61.9 (± 13.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Half-Life (t½) of Sugammadex [Part A]

End point title	Plasma Half-Life (t½) of Sugammadex [Part A][5]

End point description:

The t½ of sugammadex, defined as the time required for the plasma concentration to decrease to 50% of maximum, was determined in each Part A arm. All participants with ≥5 post-dosing samples available are included.

End point type	Primary

End point timeframe:

2 minutes (min), 15 min, 30 min, 60 min, 4-6 hours (hrs), and 10 hrs post-dose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part A: Sugammadex 2 mg (2 to <6 years)	Part A: Sugammadex 2 mg (6 to <12 years)	Part A: Sugammadex 2 mg (12 to <17 years)	Part A: Sugammadex 4 mg (2 to <6 years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	5	4	8
Units: Hours				
median (full range (min-max))	1.15 (0.964 to 1.64)	1.19 (1.01 to 1.71)	1.49 (1.17 to 1.91)	1.12 (0.922 to 1.78)

End point values	Part A: Sugammadex 4 mg (6 to <12 years)	Part A: Sugammadex 4 mg (12 to <17 years)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6		
Units: Hours				
median (full range (min-max))	1.56 (1.21 to 3.06)	1.51 (1.20 to 1.91)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with ≥1 Adverse Event (AE) [Parts A and B]

End point title	Percentage of Participants with ≥1 Adverse Event (AE) [Parts A and B][6][7]

End point description:

The percentage of participants with ≥1 AE(s) for up to 7 days after treatment was determined for each treatment group, pooled according to treatment received. An AE is defined as 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. Each participant who received a dose of study drug is included.

End point type	Primary

End point timeframe:

Up to 7 days

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Per protocol, only descriptive statistics are presented.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part B: Neostigmine + (Glycopyrrolate or Atropine)	Parts A and B: Sugammadex 2 mg	Parts A and B: Sugammadex 4 mg	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	34	51	191	
Units: Percentage of Participants				
number (not applicable)	97.1	78.4	74.9	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Recovery of Participant Train-of-Four (TOF) Ratio to ≥0.9 [Part B]

End point title	Time to Recovery of Participant Train-of-Four (TOF) Ratio to ≥0.9 [Part B][8]

End point description:

The time to recovery of TOF ratio to ≥0.9 after administration of study intervention was determined for each Part B arm. The TOF ratio is the ratio of the magnitude of the fourth (T4) and first (T1) thumb twitches elicited by 4 electrical stimulations of the ulnar nerve, indicating the current degree of NMB as a decimal from 0 (loss of T4 twitch) to 1 (no NMB). Values closer to 1 indicate less NMB. All randomized participants in Part B who received ≥1 dose of study drug are included. Per protocol, the efficacy analysis is based on comparison of the Part B: Sugammadex 2 mg arm versus the Part B: Neostigmine + (Glycopyrrolate or Atropine) arm.

End point type	Primary

End point timeframe:

Up to 30 minutes post-dose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part B: Sugammadex 2 mg/kg	Part B: Sugammadex 4 mg/kg	Part B: Neostigmine + (Glycopyrrolate or Atropine)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	169	34	
Units: Minutes				
geometric mean (confidence interval 95%)	1.6 (1.3 to 2.0)	1.9 (1.7 to 2.2)	7.5 (5.6 to 10.0)	

Statistical analyses

Statistical analysis title	Ratio of Geometric Means
Comparison groups	Part B: Sugammadex 2 mg/kg v Part B: Neostigmine + (Glycopyrrolate or Atropine)
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA
Parameter estimate	GM Ratio (SUG 2 mg / NEO + [GLY or ATR])
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.32

Secondary: Time to Recovery of Participant TOF Ratio to ≥0.7 [Part B]

End point title	Time to Recovery of Participant TOF Ratio to ≥0.7 [Part B][9]

End point description:

The time to recovery of TOF ratio to ≥0.7 after administration of study intervention was determined for each Part B arm. The TOF ratio is the ratio of the magnitude of the fourth (T4) and first (T1) thumb twitches elicited by 4 electrical stimulations of the ulnar nerve, indicating the current degree of NMB as a decimal from 0 (loss of T4 twitch) to 1 (no NMB). Values closer to 1 indicate less NMB. All randomized participants in Part B who received ≥1 dose of study drug are included.

End point type	Secondary

End point timeframe:

Up to 30 minutes post-dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per protocol, only descriptive statistics are presented.

End point values	Part B: Sugammadex 2 mg/kg	Part B: Sugammadex 4 mg/kg	Part B: Neostigmine + (Glycopyrrolate or Atropine)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	169	34	
Units: Minutes				
geometric mean (confidence interval 95%)	1.1 (0.9 to 1.3)	1.3 (1.1 to 1.4)	3.7 (2.9 to 4.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Recovery of Participant TOF Ratio to ≥0.8 [Part B]

End point title	Time to Recovery of Participant TOF Ratio to ≥0.8 [Part B][10]

End point description:

The time to recovery of TOF ratio to ≥0.8 after administration of study intervention was determined for each Part B arm. The TOF ratio is the ratio of the magnitude of the fourth (T4) and first (T1) thumb twitches elicited by 4 electrical stimulations of the ulnar nerve, indicating the current degree of NMB as a decimal from 0 (loss of T4 twitch) to 1 (no NMB). Values closer to 1 indicate less NMB. All randomized participants in Part B who received ≥1 dose of study drug are included.

End point type	Secondary

End point timeframe:

Up to 30 minutes post-dose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, only descriptive statistics are presented.

End point values	Part B: Sugammadex 2 mg/kg	Part B: Sugammadex 4 mg/kg	Part B: Neostigmine + (Glycopyrrolate or Atropine)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	169	34	
Units: Minutes				
geometric mean (confidence interval 95%)	1.3 (1.1 to 1.6)	1.5 (1.3 to 1.7)	5.0 (3.8 to 6.7)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 14 days

Adverse event reporting additional description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. All participants who received ≥1 dose of study drug are included.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Part A: Sugammadex 2 mg (2 to <6 years)
Reporting group description: -	
Reporting group title	Part A: Sugammadex 2 mg (6 to <12 years)
Reporting group description: -	
Reporting group title	Part A: Sugammadex 2 mg (12 to <17 years)
Reporting group description: -	
Reporting group title	Part A: Sugammadex 4 mg (2 to <6 years)
Reporting group description: -	
Reporting group title	Part A: Sugammadex 4 mg (6 to <12 years)
Reporting group description: -	
Reporting group title	Part B: Sugammadex 2 mg
Reporting group description: -	
Reporting group title	Part A: Sugammadex 4 mg (12 to <17 years)
Reporting group description: -	
Reporting group title	Part B: Sugammadex 4 mg
Reporting group description: -	
Reporting group title	Part B: Neostigmine + (Glycopyrrolate or Atropine)

Reporting group description: -

Serious adverse events	Part A: Sugammadex 2 mg (2 to <6 years)	Part A: Sugammadex 2 mg (6 to <12 years)	Part A: Sugammadex 2 mg (12 to <17 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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

Post procedural bile leak			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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			
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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			
Laryngospasm			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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			
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (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

Serious adverse events	Part A:	Part A:	Part B:

	Sugammadex 4 mg (2 to <6 years)	Sugammadex 4 mg (6 to <12 years)	Sugammadex 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	3 / 33 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (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
Post procedural bile leak			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (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 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (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			
Laryngospasm			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (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			

Urinary tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (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

Serious adverse events	Part A: Sugammadex 4 mg (12 to <17 years)	Part B: Sugammadex 4 mg	Part B: Neostigmine + (Glycopyrrolate or Atropine)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	3 / 169 (1.78%)	2 / 34 (5.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 169 (0.59%)	0 / 34 (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
Post procedural bile leak			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (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			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 169 (0.59%)	0 / 34 (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
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 169 (0.59%)	0 / 34 (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
Respiratory, thoracic and mediastinal disorders			
Laryngospasm			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part A: Sugammadex 2 mg (2 to <6 years)	Part A: Sugammadex 2 mg (6 to <12 years)	Part A: Sugammadex 2 mg (12 to <17 years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 9 (88.89%)	3 / 5 (60.00%)	2 / 4 (50.00%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Cardiac procedure complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Incision site pain			

subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Incision site swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Postoperative respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	4 / 9 (44.44%)	3 / 5 (60.00%)	1 / 4 (25.00%)
occurrences (all)	4	3	1
Procedural site reaction			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Procedural vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Pericardial effusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Mouth swelling			
subjects affected / exposed	0 / 9 (0.00%)	2 / 5 (40.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Palatal swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	1 / 5 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	2 / 9 (22.22%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Postoperative wound infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 5 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part A: Sugammadex 4 mg (2 to <6 years)	Part A: Sugammadex 4 mg (6 to <12 years)	Part B: Sugammadex 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)	5 / 6 (83.33%)	26 / 33 (78.79%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Cardiac procedure complication			
subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Incision site pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
Incision site swelling			

subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Postoperative respiratory failure			
subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Procedural nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
Procedural pain			
subjects affected / exposed	7 / 10 (70.00%)	3 / 6 (50.00%)	22 / 33 (66.67%)
occurrences (all)	7	3	22
Procedural site reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Procedural vomiting			
subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 6 (16.67%)	1 / 33 (3.03%)
occurrences (all)	1	1	1
Pericardial effusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Eye irritation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Mouth swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 6 (0.00%)	1 / 33 (3.03%)
occurrences (all)	1	0	1
Palatal swelling			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 6 (16.67%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 6 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part A: Sugammadex 4 mg (12 to <17 years)	Part B: Sugammadex 4 mg	Part B: Neostigmine + (Glycopyrrolate or Atropine)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	117 / 169 (69.23%)	29 / 34 (85.29%)
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 169 (0.59%)	2 / 34 (5.88%)
occurrences (all)	0	1	2
Injury, poisoning and procedural complications			
Cardiac procedure complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Incision site pain			
subjects affected / exposed	0 / 6 (0.00%)	5 / 169 (2.96%)	1 / 34 (2.94%)
occurrences (all)	0	5	1
Incision site swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Postoperative respiratory failure			

subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	0 / 6 (0.00%)	9 / 169 (5.33%)	0 / 34 (0.00%)
occurrences (all)	0	9	0
Procedural pain			
subjects affected / exposed	3 / 6 (50.00%)	98 / 169 (57.99%)	24 / 34 (70.59%)
occurrences (all)	3	109	25
Procedural site reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Procedural vomiting			
subjects affected / exposed	0 / 6 (0.00%)	4 / 169 (2.37%)	1 / 34 (2.94%)
occurrences (all)	0	4	1
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 6 (16.67%)	9 / 169 (5.33%)	3 / 34 (8.82%)
occurrences (all)	1	9	3
Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 169 (0.59%)	2 / 34 (5.88%)
occurrences (all)	0	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 169 (1.18%)	1 / 34 (2.94%)
occurrences (all)	0	2	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 169 (0.59%)	2 / 34 (5.88%)
occurrences (all)	0	1	3
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 169 (0.59%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 169 (0.59%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Mouth swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	10 / 169 (5.92%)	2 / 34 (5.88%)
occurrences (all)	1	10	2
Palatal swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	20 / 169 (11.83%)	2 / 34 (5.88%)
occurrences (all)	0	22	2
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	3 / 169 (1.78%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	2 / 169 (1.18%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			

subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 169 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2017	AM1: The primary purposes of the amendment were to update safety definitions regarding treatment-emergent bradycardia and to add text regarding trial stopping criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported