Reversal of Neuromuscular Blockade With Sugammadex or Usual Care in Hip Fracture Surgery or Joint (Hip/Knee) Replacement (P07038)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT01422304

First received: August 22, 2011
Last updated: September 3, 2015
Last verified: September 2015
History of Changes

Purpose

This study will assess the effect of reversal of neuromuscular blockade with sugammadex compared with reversal according to usual care (neostigmine or spontaneous reversal) on the incidence of post-surgical bleeding events and on coagulation parameters in participants undergoing hip fracture surgery or joint (hip/knee) replacement surgery with neuromuscular blockage induced by rocuronium or vecuronium.

Condition	Intervention	Phase
Neuromuscular Blockade Arthroplasty, Replacement, Hip Arthroplasty, Replacement, Knee Blood Coagulation Antithrombotic Agents	Drug: Sugammadex Drug: neostigmine and glycopyrrolate or atropine Drug: Placebo to neostigmine Drug: Placebo to sugammadex	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: A Randomized, Controlled, Parallel-group, Double-blind Trial of Sugammadex or Usual Care (Neostigmine or Spontaneous Recovery) for Reversal of Rocuronium- or Vecuronium-induced Neuromuscular Blockade in Patients Receiving Thromboprophylaxis and Undergoing Hip Fracture Surgery or Joint (Hip/Knee) Replacement (Protocol No. P07038)

Resource links provided by NLM:

MedlinePlus related topics: Fractures Hip Injuries and Disorders

Drug Information available for: Atropine Neostigmine methylsulfate Glycopyrrolate Sugammadex Sugammadex sodium

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 24 Hours After Study Drug Administration [Time Frame: Up to 24 hours post study drug administration] [Designated as safety issue: Yes]

  Post-treatment events of bleeding were evaluated by a medically-qualified, blinded member of the surgical team (Blinded Safety Assessor), in consultation with the surgeon, to determine if an event was a "suspected, unanticipated adverse event of bleeding" (SUAEB). A SUAEB is an event of bleeding outside the usual boundaries of expectations for a participant (e.g., in amount of blood lost, prolonged duration of bleeding, or other factors) considering the type of procedure as well as participant's specific surgical experience and underlying risk of bleeding. In addition, blinded review of clinical and laboratory databases was performed to identify any event potentially consistent with a SUAEB; these were reviewed by the Blinded Safety Assessor, who determined if any was a SUAEB. All SUAEBs were evaluated by a blinded external Adjudication Committee, which classified each as either: 1) a major bleeding event, 2) a non-major bleeding event, or 3) not an unanticipated event of bleeding.

Secondary Outcome Measures:

- Percent Change From Baseline in Activated Partial Thromboplastin Time (aPTT) at 10 and 60 Minutes Post Study Drug Administration [Time Frame: Baseline, 10 and 60 minutes post study drug administration] [Designated as safety issue: Yes]

  Change from baseline in aPTT is identified in study protocol as the Key Secondary Outcome Measure. Blood samples for determination of aPTT values were obtained at baseline and at 10 and 60 minutes after study drug administration. aPTT is a performance indicator measuring the efficacy of the intrinsic and common blood coagulation (blood clotting) pathways. Higher values of aPTT indicate a reduction in the clotting tendency of blood.

- Percent Change From Baseline in Prothrombin Time (International Normalized Ratio) (PT[INR]) at 10 and 60 Minutes Post Study Drug Administration [Time Frame: Baseline, 10 and 60 minutes post study drug administration] [Designated as safety issue: Yes]

  Change from baseline in PT(INR) is identified in study protocol as an Other Secondary Outcome Measure. Blood samples for determination of PT(INR) values were obtained at baseline and at 10 and 60 minutes after study drug administration. PT(INR) is a performance indicator measuring the efficacy of the extrinsic and common blood coagulation (blood clotting) pathways. The INR is the ratio of a participant's prothrombin time to a normal (control) sample, raised to the power of the International Sensitivity Index (ISI) value for the analytical system used (INR = [PT-Test/PT-Normal]^ISI). Higher values of PT(INR) indicate a reduction in the clotting tendency of blood.

- Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration] [Designated as safety issue: Yes]

  This Measure is identified in study protocol as an Other Secondary Outcome Measure. Post-treatment events of bleeding were evaluated by a medically-qualified, blinded member of the surgical team (Blinded Safety Assessor), in consultation with the surgeon, to determine if an event was a "suspected, unanticipated adverse event of bleeding" (SUAEB). A SUAEB is an event of bleeding outside the usual boundaries of expectations for a participant considering the type of procedure as well as participant's specific surgical experience and underlying risk of bleeding. In addition, blinded review of clinical and laboratory databases was performed to identify any event potentially consistent with a SUAEB; these were reviewed by the Blinded Safety Assessor, who determined if any was a SUAEB. All SUAEBs were evaluated by a blinded external Adjudication Committee, which classified each as either: 1) a major bleeding event, 2) a non-major bleeding event, or 3) not an unanticipated event of bleeding.

- Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 24 Hours After Study Drug Administration [Time Frame: Up to 24 hours post study drug administration] [Designated as safety issue: Yes]

  This Measure is identified in study protocol as an Other Secondary Outcome Measure. All SUAEB were evaluated by a blinded external Adjudication Committee. Major bleeding event (MBE) = one or more of the following: 1) Fatal bleeding; 2) Bleeding that is symptomatic and occurs in critical area/organ, in a non-operated joint, or is intramuscular with compartment syndrome; 3) Extrasurgical site bleeding causing a fall in hemoglobin (Hgb) level of 20 g/L (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red blood cells (RBCs), occurring within 24 hours of the bleeding; 4) Surgical site bleeding requiring second intervention, or bleeding at operated joint that interferes with rehabilitation; or 5) Surgical site bleeding that is unexpected/prolonged and/or causes hemodynamic instability, with fall in Hgb level of at least 20 g/L (1.24 mmol/L) or transfusion of at least two units of whole blood or RBCs, occurring within 24 hours of the bleeding.

- Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration] [Designated as safety issue: Yes]

  This Measure is identified in study protocol as an Other Secondary Outcome Measure. All SUAEB were evaluated by a blinded external Adjudication Committee. MBE = one or more of the following: 1) Fatal bleeding; 2) Bleeding that is symptomatic and occurs in critical

area/organ, in a non-operated joint, or is intramuscular with compartment syndrome; 3) Extrasurgical site bleeding causing a fall in Hgb level of 20 g/L (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or RBCs, occurring within 24 hours of the bleeding; 4) Surgical site bleeding requiring second intervention, or bleeding at operated joint that interferes with rehabilitation; or 5) Surgical site bleeding that is unexpected/prolonged and/or causes hemodynamic instability, with fall in Hgb level of at least 20 g/L (1.24 mmol/L) or transfusion of at least two units of whole blood or RBCs, occurring within 24 hours of the bleeding.

- Number of Participants With One or More Adjudicated Venous Thromboembolic (VTE) Events With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration] [Designated as safety issue: Yes]

  This Measure is identified in study protocol as an Other Secondary Outcome Measure. Suspected symptomatic VTE events were evaluated by a blinded external Adjudication Committee. The confirmation of a VTE event was based on determination of a clinically meaningful venous thrombosis (e.g., pulmonary embolism or deep vein thrombosis).

- Number of Participants With One or More Adjudicated Events of Anaphylaxis With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration] [Designated as safety issue: Yes]

  This Measure is identified in study protocol as an Other Secondary Outcome Measure. Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death. Adverse events suggestive of hypersensitivity which met defined criteria (e.g., serious event) and/or suspected events of anaphylaxis were evaluated by a blinded external Adjudication Committee to determine whether such events met either of the following two criteria for anaphylaxis (Sampson et al. J Allergy Clin Immunol 2006;117:391-7) - 1. Acute onset of an illness with involvement of the skin, mucosal tissue or both, and at least one of the following: a) respiratory compromise, b) reduced blood pressure (BP) or associated symptoms of end-organ dysfunction. 2. Two or more of the following that occur rapidly after exposure to a likely allergen for that participant: a) involvement of the skin-mucosal tissue, b) respiratory compromise, c) reduced BP or associated symptoms, d) persistent gastrointestinal symptoms.

Other Outcome Measures:

- Postoperative Drainage Volume Within 24 Hours After Study Drug Administration [Time Frame: Up to 24 hours post study drug administration] [Designated as safety issue: Yes]

  The total volume of postoperative drainage from the surgical site over the 24 hours after study drug administration was recorded.

- Number of Participants Requiring Any Postoperative Transfusion [Time Frame: From end of study drug administration through approximately 120 hours after study drug administration] [Designated as safety issue: Yes]

  The number of participants who received a transfusion unit (e.g., whole blood, packed RBCs, cell saver RBCs, fresh frozen plasma, platelets) that started after study drug administration and within 120 hours after study drug administration (or within 48 hours after any previous [i.e., predose] transfusion for participants who had received a previous transfusion) was determined.

- Total Transfusion Volume in Participants Who Required Postoperative Transfusion [Time Frame: From end of study drug administration through approximately 120 hours after study drug administration] [Designated as safety issue: Yes]

  Among participants who received a transfusion unit (e.g., whole blood, packed RBCs, cell saver RBCs, fresh frozen plasma, platelets) that started after study drug administration and within 120 hours after study drug administration (or within 48 hours after any previous [i.e., predose] transfusion for participants who had received a previous transfusion), the total volume of blood transfused post study drug was calculated. The volume of blood transfused post study drug (using linear interpolation when transfusions were ongoing at the time of study drug administration) was converted to grams of Hgb transfused, using RBC concentration information received from the investigators. The sum of Hgb transfused was standardized to "normal" volume Hgb in homologous whole blood, using 20 g/dL Hgb for calculation of the standardized volume.

- Postoperative Changes in Hgb Concentrations Using the Bleeding Index [Time Frame: Baseline and Visit 3 (24-48 hours post study drug administration)] [Designated as safety issue: Yes]

  The Bleeding Index was used to describe postoperative changes in Hgb concentrations at Visit 3. Bleeding Index = Hgb level at Visit 3 - Hgb level at baseline, adjusted for the amount of RBCs transfused. Missing baseline Hgb values were imputed using the overall mean Hgb value at baseline.

- Number of Participants With One or More Postoperative Anemia Adverse Events With Onset Within 72 Hours After Study Drug Administration [Time Frame: Up to 72 hours post study drug administration] [Designated as safety issue: Yes]

  This measure is the incidence of postoperative anaemia with an onset within 72 hours after study drug administration. A participant is included in the count for this measure if an adverse event with any of the following event terms occurred in the participant with onset within the defined time frame: postoperative anaemia, anaemia, haemorrhagic anaemia, haemoglobin decreased or haemoglobin S decreased.

Enrollment: 1198

Study Start Date:	October 2011
Study Completion Date:	September 2012
Primary Completion Date:	September 2012 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Sugammadex Prior to randomization, participants will be assigned to planned active reversal or planned spontaneous recovery by the anesthesiologist according to the recovery method the anesthesiologist would have chosen if the participant were not in the study. In this treatment arm, participants assigned to planned active reversal will receive sugammadex and placebo to neostigmine, and participants assigned to planned spontaneous recovery will receive sugammadex. Study drug will be administered after the last dose of rocuronium or vecuronium and after wound closure.	Drug: Sugammadex Sugammadex 4 mg/kg intravenously Other Name: SCH 900616, MK-8616 Drug: Placebo to neostigmine Normal saline (NaCl 0.9%)
Experimental: Usual Care Prior to randomization, participants will be assigned to planned active reversal or planned spontaneous recovery by the anesthesiologist according to the recovery method the anesthesiologist would have chosen if the participant were not in the study. In this treatment arm, participants assigned to planned active reversal will receive neostigmine and placebo to sugammadex, and participants assigned to planned spontaneous recovery will receive placebo to sugammadex. Study drug will be administered after the last dose of rocuronium or vecuronium and after wound closure.	Drug: neostigmine and glycopyrrolate or atropine Neostigmine and glycopyrrolate or neostigmine and atropine administered intravenously per usual practice and per the product labels Drug: Placebo to sugammadex Normal saline (NaCl 0.9%)

Detailed Description:

Participants will be randomized to sugammadex or usual care in a 1:1 ratio.

Eligibility

Ages Eligible for Study:	18 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Must be American Society of Anesthesiologists (ASA) Class 1, 2, or 3
- Must be scheduled for a hip fracture surgery or joint (hip or knee) replacement surgery under general anesthesia including the use of rocuronium or vecuronium for neuromuscular blockade
- Must be:
  - Currently receiving thromboprophylactic (anti-clotting) therapy with low molecular weight heparin (LMWH) or unfractionated heparin (UFH), or
  - Planned to initiate thromboprophylactic therapy with LMWH or UFH prior to or during surgery, or
  - Currently receiving ongoing thromboprophylactic therapy with a vitamin K antagonist that has been temporarily substituted with peri-operative LMWH or UFH, and/or
  - Currently receiving ongoing thromboprophylactic therapy with low-dose aspirin or other antiplatelet therapy
- Platelet count above the lower limit of normal range
- Appropriate candidate for rapid reversal of neuromuscular blockade
- Sexually active females must agree to use a medically accepted method of contraception through seven days after receiving protocol-specified medication

Exclusion Criteria:

- Anatomical malformations that may lead to difficult intubation

- Neuromuscular disorder that may affect neuromuscular blockade
- History of a coagulation disorder, bleeding diathesis, systemic lupus erythematosus or antiphospholipid syndrome
- History or evidence of active abnormal bleeding or blood clotting within 30 days prior to screening
- Significant hepatic dysfunction
- Severe renal insufficiency
- History or family history of malignant hyperthermia
- Hypersensitivity or hypersensitivity-like reaction to sugammadex, muscle relaxants, or other medications used during general anesthesia
- Planned intravenous administration of toremifene and/or fusidic acid within 24 hours before or within 24 hours after study medication
- Recent, severe trauma
- Body Mass Index (BMI) > 35
- Any contraindication to administration of sugammadex or neostigmine/glycopyrrolate (or neostigmine/atropine)
- Pregnant or intends to become pregnant between randomization and the Day 30 follow-up visit
- Breast-feeding
- Previously treated with sugammadex or participated in a sugammadex clinical trial
- Has an active hip/knee infection and is scheduled for revision surgery

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

No Contacts or Locations Provided

More Information

No publications provided

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT01422304 History of Changes
Other Study ID Numbers:	P07038 2011-001201-27 MK-8616-059
Study First Received:	August 22, 2011
Results First Received:	August 19, 2013
Last Updated:	September 3, 2015
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices

Additional relevant MeSH terms:

Hip Fractures	Cholinergic Antagonists
Femoral Fractures	Cholinesterase Inhibitors
Fractures, Bone	Enzyme Inhibitors
Hip Injuries	Molecular Mechanisms of Pharmacological Action
Leg Injuries	Muscarinic Antagonists
Wounds and Injuries	Neurotransmitter Agents
Glycopyrrolate	Parasympathomimetics
Neostigmine	Peripheral Nervous System Agents
Adjuvants, Anesthesia	Pharmacologic Actions
Autonomic Agents	Physiological Effects of Drugs
Central Nervous System Agents	Therapeutic Uses
Cholinergic Agents	

ClinicalTrials.gov processed this record on April 07, 2016

TO TOP

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ClinicalTrials.gov Identifier:
NCT01422304

First received: August 22, 2011
Last updated: September 3, 2015
Last verified: September 2015
History of Changes

Results First Received: August 19, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Conditions:	Neuromuscular Blockade Arthroplasty, Replacement, Hip Arthroplasty, Replacement, Knee Blood Coagulation Antithrombotic Agents
Interventions:	Drug: Sugammadex Drug: neostigmine and glycopyrrolate or atropine Drug: Placebo to neostigmine Drug: Placebo to sugammadex

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Participant Flow: Overall Study

	Sugammadex	Usual Care
STARTED	**598** [1]	**600** [1]
Treated	**595**	**589** [2]
COMPLETED	**574**	**563**
NOT COMPLETED	**24**	**37**
Adverse Event	**0**	**1**
Lost to Follow-up	**14**	**20**
Never Entered Follow-up	**2**	**1**
Protocol Violation	**1**	**0**
Withdrawal by Subject	**4**	**2**
Did Not Meet Protocol Eligibility	**0**	**2**
Not Treated	**3**	**11**

[1] Randomized

[2] 1 given sugammadex; thus All Participants as Treated (APaT) Ns are 596 Sugammadex, 588 Usual Care

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV)

	administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).
Total	Total of all reporting groups

Baseline Measures

	Sugammadex	Usual Care	Total
Number of Participants [units: participants]	**596**	**588**	**1184**
Age [units: years] Mean (Standard Deviation)	**66.7 (12.0)**	**66.6 (11.3)**	**66.7 (11.7)**
Gender [units: participants]			
Female	**326**	**340**	**666**
Male	**270**	**248**	**518**
Activated Partial Thromboplastin Time (aPTT) [1] [units: seconds] Mean (Standard Deviation)	**31.14 (4.38)**	**31.01 (4.14)**	**31.08 (4.26)**
Prothrombin Time (International Normalized Ratio) (PT[INR]) [2] [units: ratio] Mean (Standard Deviation)	**1.121 (0.159)**	**1.114 (0.132)**	**1.117 (0.147)**

[1] n=556, 535, 1091 for Sugammadex, Usual Care and Total, respectively
[2] n=557, 535, 1092 for Sugammadex, Usual Care and Total, respectively

Outcome Measures

Hide All Outcome Measures

1. Primary: Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 24 Hours After Study Drug Administration [Time Frame: Up to 24 hours post study drug administration]

Measure Type	Primary
Measure Title	Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 24 Hours After Study Drug Administration
Measure Description	Post-treatment events of bleeding were evaluated by a medically-qualified, blinded member of the surgical team (Blinded Safety Assessor), in consultation with the surgeon, to determine if an event was a "suspected, unanticipated adverse event of bleeding" (SUAEB). A SUAEB is an event of bleeding outside the usual boundaries of expectations for a participant (e.g., in amount of blood lost, prolonged duration of bleeding, or other factors) considering the type of procedure as well as participant's specific surgical experience and underlying risk of bleeding. In addition, blinded review of clinical and laboratory databases was performed to identify any event potentially consistent with a SUAEB; these were reviewed by the Blinded Safety Assessor, who determined if any was a SUAEB. All SUAEBs were evaluated by a blinded external Adjudication Committee, which classified each as either: 1) a major bleeding event, 2) a non-major bleeding event, or 3) not an unanticipated event of bleeding.

Time Frame	Up to 24 hours post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 24 Hours After Study Drug Administration [units: participants]	**17**	**24**

Statistical Analysis 1 for Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 24 Hours After Study Drug Administration

Groups [1]	All groups
Method [2]	Cochran-Mantel-Haenszel
Risk Ratio (RR) [3]	0.70
95% Confidence Interval	0.38 to 1.29

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Cochran-Mantel-Haenszel method was stratified for renal function (estimated creatinine clearance < or ≥ 60 mL/min) and prophylactic antithrombotic therapy (including low molecular weight heparin [LMWH], including unfractionated heparin [UFH], or not including either LMWH or UFH)
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Relative risk is Sugammadex versus Usual Care

2. Secondary: Percent Change From Baseline in Activated Partial Thromboplastin Time (aPTT) at 10 and 60 Minutes Post Study Drug Administration [Time Frame: Baseline, 10 and 60 minutes post study drug administration]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Activated Partial Thromboplastin Time (aPTT) at 10 and 60 Minutes Post Study Drug Administration
Measure Description	Change from baseline in aPTT is identified in study protocol as the Key Secondary Outcome Measure. Blood samples for determination of aPTT values were obtained at baseline and at 10 and 60 minutes after study drug administration. aPTT is a performance indicator measuring the efficacy of the intrinsic and common blood coagulation (blood clotting) pathways. Higher values of aPTT indicate a reduction in the clotting tendency of blood.
Time Frame	Baseline, 10 and 60 minutes post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants in APaT population who had baseline and at least one post baseline aPTT measurement within defined assessment window (10 or 60 minutes post study drug).

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**556**	**535**
Percent Change From Baseline in Activated Partial Thromboplastin Time (aPTT) at 10 and 60 Minutes Post Study Drug Administration [units: percent change] Mean (Standard Deviation)		
10 minutes (Sugammadex n=525, Usual Care n=507)	**6.0 (22.4)**	**-0.1 (13.6)**
60 minutes (Sugammadex n=523, Usual Care n=505)	**0.4 (29.1)**	**-1.2 (22.7)**

Statistical Analysis 1 for Percent Change From Baseline in Activated Partial Thromboplastin Time (aPTT) at 10 and 60 Minutes Post Study Drug

Administration

Groups [1]	All groups
Method [2]	Constrained Longitudinal Data Analysis
Geometric Mean Ratio (GMR) (%) [3]	5.5
95% Confidence Interval	3.7 to 7.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Model was restricted to have no difference between treatment groups for baseline assessment, and was adjusted for center, usual care group (active reversal or spontaneous recovery), renal function (estimated creatinine clearance < or ≥ 60 mL/min), prophylactic antithrombotic therapy (including LMWH, including UFH, or not including either LMWH or UFH), type of hip/knee surgical procedure, and the interaction of time by treatment.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model included those in APaT population with any baseline or post baseline aPTT value in 10 or 60 minute window (Sugammadex, Usual Care N=567, 548)
[3]	Other relevant estimation information:
	Estimate of difference in Sugammadex versus Usual Care change from baseline at 10 minutes post dose calculated with log of aPTT values as dependent variable. Results transformed back to GMR of respective changes (expressed as %, = [GMR – 1]*100).

Statistical Analysis 2 for Percent Change From Baseline in Activated Partial Thromboplastin Time (aPTT) at 10 and 60 Minutes Post Study Drug Administration

Groups [1]	All groups
Method [2]	Constrained Longitudinal Data Analysis
GMR (%) [3]	0.9
95% Confidence Interval	-0.9 to 2.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Model was restricted to have no difference between treatment groups for baseline assessment, and was adjusted for center, usual care group (active reversal or spontaneous recovery), renal function (estimated creatinine clearance < or ≥ 60 mL/min), prophylactic antithrombotic therapy (including LMWH, including UFH, or not including either LMWH or UFH), type of hip/knee surgical procedure, and the interaction of time by treatment.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model included those in APaT population with any baseline or post baseline aPTT value in 10 or 60 minute window (Sugammadex, Usual Care N=567, 548)
[3]	Other relevant estimation information:
	Estimate of difference in Sugammadex versus Usual Care change from baseline at 60 minutes post dose calculated with log of aPTT values as dependent variable. Results transformed back to GMR of respective changes (expressed as %, = [GMR – 1]*100).

3. Secondary: Percent Change From Baseline in Prothrombin Time (International Normalized Ratio) (PT[INR]) at 10 and 60 Minutes Post Study Drug Administration [Time Frame: Baseline, 10 and 60 minutes post study drug administration]

Measure Type	Secondary
Measure Title	Percent Change From Baseline in Prothrombin Time (International Normalized Ratio) (PT[INR]) at 10 and 60 Minutes Post Study Drug Administration

Measure Description	Change from baseline in PT(INR) is identified in study protocol as an Other Secondary Outcome Measure. Blood samples for determination of PT(INR) values were obtained at baseline and at 10 and 60 minutes after study drug administration. PT(INR) is a performance indicator measuring the efficacy of the extrinsic and common blood coagulation (blood clotting) pathways. The INR is the ratio of a participant's prothrombin time to a normal (control) sample, raised to the power of the International Sensitivity Index (ISI) value for the analytical system used (INR = [PT-Test/PT-Normal]^ISI). Higher values of PT(INR) indicate a reduction in the clotting tendency of blood.
Time Frame	Baseline, 10 and 60 minutes post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants in APaT population who had baseline and at least one post baseline PT(INR) measurement within defined assessment window (10 or 60 minutes post study drug).

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**557**	**535**
Percent Change From Baseline in Prothrombin Time (International Normalized Ratio) (PT[INR]) at 10 and 60 Minutes Post Study Drug Administration [units: percent change] Mean (Standard Deviation)		
10 minutes (Sugammadex n=526, Usual Care n=507)	**8.0 (63.4)**	**2.5 (14.3)**
60 minutes (Sugammadex n=524, Usual Care n=505)	**8.9 (79.8)**	**3.4 (23.2)**

Statistical Analysis 1 for Percent Change From Baseline in Prothrombin Time (International Normalized Ratio) (PT[INR]) at 10 and 60 Minutes Post Study Drug Administration

Groups [1]	All groups
Method [2]	Constrained Longitudinal Data Analysis
GMR (%) [3]	3.0
95% Confidence Interval	1.3 to 4.7

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Model was restricted to have no difference between treatment groups for baseline assessment, and was adjusted for center, usual care group (active reversal or spontaneous recovery), renal function (estimated creatinine clearance < or ≥ 60 mL/min), prophylactic antithrombotic therapy (including LMWH, including UFH, or not including either LMWH or UFH), type of hip/knee surgical procedure, and the interaction of time by treatment.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model included those in APaT population with any baseline or post baseline PT(INR) value in 10 or 60 minute window (Sugammadex, Usual Care N=567, 548)
[3]	Other relevant estimation information:
	Estimate of difference in Sugammadex versus Usual Care change from baseline at 10 minutes post dose calculated with log of PT(INR) values as dependent variable. Results transformed back to GMR of respective changes (expressed as %, = [GMR – 1]*100).

Statistical Analysis 2 for Percent Change From Baseline in Prothrombin Time (International Normalized Ratio) (PT[INR]) at 10 and 60 Minutes Post Study Drug Administration

Groups [1]	All groups
Method [2]	Constrained Longitudinal Data Analysis
GMR (%) [3]	0.9
95% Confidence Interval	-1.0 to 2.9

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Model was restricted to have no difference between treatment groups for baseline assessment, and was adjusted for center, usual care group (active reversal or spontaneous recovery), renal function (estimated creatinine clearance < or ≥ 60 mL/min), prophylactic antithrombotic therapy (including LMWH, including UFH, or not including either LMWH or UFH), type of hip/knee surgical procedure, and the interaction of time by treatment.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	Model included those in APaT population with any baseline or post baseline PT(INR) value in 10 or 60 minute window (Sugammadex, Usual Care N=567, 548)
[3]	Other relevant estimation information:
	Estimate of difference in Sugammadex versus Usual Care change from baseline at 60 minutes post dose calculated with log of PT(INR) values as dependent variable. Results transformed back to GMR of respective changes (expressed as %, = [GMR – 1]*100).

4. Secondary: Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration]

Measure Type	Secondary
Measure Title	Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 14 Days After Study Drug Administration
Measure Description	This Measure is identified in study protocol as an Other Secondary Outcome Measure. Post-treatment events of bleeding were evaluated by a medically-qualified, blinded member of the surgical team (Blinded Safety Assessor), in consultation with the surgeon, to determine if an event was a "suspected, unanticipated adverse event of bleeding" (SUAEB). A SUAEB is an event of bleeding outside the usual boundaries of expectations for a participant considering the type of procedure as well as participant's specific surgical experience and underlying risk of bleeding. In addition, blinded review of clinical and laboratory databases was performed to identify any event potentially consistent with a SUAEB; these were reviewed by the Blinded Safety Assessor, who determined if any was a SUAEB. All SUAEBs were evaluated by a blinded external Adjudication Committee, which classified each as either: 1) a major bleeding event, 2) a non-major bleeding event, or 3) not an unanticipated event of bleeding.

Time Frame	Up to 14 days post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 14 Days After Study Drug Administration [units: participants]	**24**	**27**

Statistical Analysis 1 for Number of Participants With One or More Adjudicated Events of Bleeding (Major or Non-major) With Onset Within 14 Days After Study Drug Administration

Groups [1]	All groups
Method [2]	Miettinen and Nurminen
Risk Difference (%) [3]	-0.6
95% Confidence Interval	-3.0 to 1.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Risk difference (%) = Sugammadex incidence - Usual Care incidence

5. Secondary: Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 24 Hours After Study Drug Administration [Time Frame: Up to 24 hours post study drug administration]

Measure Type	Secondary
Measure Title	Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 24 Hours After Study Drug Administration
Measure Description	This Measure is identified in study protocol as an Other Secondary Outcome Measure. All SUAEB were evaluated by a blinded external Adjudication Committee. Major bleeding event (MBE) = one or more of the following: 1) Fatal bleeding; 2) Bleeding that is symptomatic and occurs in critical area/organ, in a non-operated joint, or is intramuscular with compartment syndrome; 3) Extrasurgical site bleeding causing a fall in hemoglobin (Hgb) level of 20 g/L (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or red blood cells (RBCs), occurring within 24 hours of the bleeding; 4) Surgical site bleeding requiring second intervention, or bleeding at operated joint that interferes with rehabilitation; or 5) Surgical site bleeding that is unexpected/prolonged and/or causes hemodynamic instability, with fall in Hgb level of at least 20 g/L (1.24 mmol/L) or transfusion of at least two units of whole blood or RBCs, occurring within 24 hours of the bleeding.
Time Frame	Up to 24 hours post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 24 Hours After Study Drug Administration [units: participants]	**12**	**20**

Statistical Analysis 1 for Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 24 Hours After Study Drug Administration

Groups [1]	All groups
Method [2]	Miettinen and Nurminen

Risk Difference (%) [3]	-1.4
95% Confidence Interval	-3.4 to 0.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Risk difference (%) = Sugammadex incidence - Usual Care incidence

6. Secondary: Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration]

Measure Type	Secondary
Measure Title	Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 14 Days After Study Drug Administration
Measure Description	This Measure is identified in study protocol as an Other Secondary Outcome Measure. All SUAEB were evaluated by a blinded external Adjudication Committee. MBE = one or more of the following: 1) Fatal bleeding; 2) Bleeding that is symptomatic and occurs in critical area/organ, in a non-operated joint, or is intramuscular with compartment syndrome; 3) Extrasurgical site bleeding causing a fall in Hgb level of 20 g/L (1.24 mmol/L) or more, or leading to transfusion of two or more units of whole blood or RBCs, occurring within 24 hours of the bleeding; 4) Surgical site bleeding requiring second intervention, or bleeding at operated joint that interferes with rehabilitation; or 5) Surgical site bleeding that is unexpected/prolonged and/or causes hemodynamic instability, with fall in Hgb level of at least 20 g/L (1.24 mmol/L) or transfusion of at least two units of whole blood or RBCs, occurring within 24 hours of the bleeding.
Time Frame	Up to 14 days post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

		Usual

	Sugammadex	Care
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 14 Days After Study Drug Administration [units: participants]	**18**	**23**

Statistical Analysis 1 for Number of Participants With One or More Adjudicated Major Events of Bleeding With Onset Within 14 Days After Study Drug Administration

Groups [1]	All groups
Method [2]	Miettinen and Nurminen
Risk Difference (%) [3]	-0.9
95% Confidence Interval	-3.1 to 1.2

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Risk difference (%) = Sugammadex incidence - Usual Care incidence

7. Secondary: Number of Participants With One or More Adjudicated Venous Thromboembolic (VTE) Events With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration]

Measure Type	Secondary
Measure Title	Number of Participants With One or More Adjudicated Venous Thromboembolic (VTE) Events With Onset Within 14 Days After Study Drug Administration
Measure Description	This Measure is identified in study protocol as an Other Secondary Outcome Measure. Suspected symptomatic VTE events were evaluated by a blinded external Adjudication Committee. The confirmation of a VTE event was based on determination of a clinically meaningful venous thrombosis (e.g., pulmonary embolism or deep vein thrombosis).
Time Frame	Up to 14 days post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of

	neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants With One or More Adjudicated Venous Thromboembolic (VTE) Events With Onset Within 14 Days After Study Drug Administration [units: participants]	**5**	**3**

Statistical Analysis 1 for Number of Participants With One or More Adjudicated Venous Thromboembolic (VTE) Events With Onset Within 14 Days After Study Drug Administration

Groups [1]	All groups
Method [2]	Miettinen and Nurminen
Risk Difference (%) [3]	0.3
95% Confidence Interval	-0.7 to 1.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Risk difference (%) = Sugammadex incidence - Usual Care incidence

8. Secondary: Number of Participants With One or More Adjudicated Events of Anaphylaxis With Onset Within 14 Days After Study Drug Administration [Time Frame: Up to 14 days post study drug administration]

Measure Type	Secondary
Measure Title	Number of Participants With One or More Adjudicated Events of Anaphylaxis With Onset Within 14 Days After Study Drug Administration
Measure Description	This Measure is identified in study protocol as an Other Secondary Outcome Measure. Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death. Adverse events suggestive of hypersensitivity which met defined criteria (e.g., serious event) and/or suspected events of anaphylaxis were evaluated by a blinded external Adjudication Committee to determine whether such events met either of the following two criteria for anaphylaxis (Sampson et al. J Allergy Clin Immunol 2006;117:391-7) - 1. Acute onset of an illness with involvement of the skin, mucosal tissue or both, and at least one of the following: a) respiratory compromise, b) reduced blood pressure (BP) or associated symptoms of end-organ dysfunction. 2. Two or more of the following that occur rapidly after exposure to a likely allergen for that participant: a) involvement of the skin-mucosal tissue, b) respiratory compromise, c) reduced BP or associated

	symptoms, d) persistent gastrointestinal symptoms.
Time Frame	Up to 14 days post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants With One or More Adjudicated Events of Anaphylaxis With Onset Within 14 Days After Study Drug Administration [units: participants]	**0**	**0**

No statistical analysis provided for Number of Participants With One or More Adjudicated Events of Anaphylaxis With Onset Within 14 Days After Study Drug Administration

9. Other Pre-specified: Postoperative Drainage Volume Within 24 Hours After Study Drug Administration [Time Frame: Up to 24 hours post study drug administration]

Measure Type	Other Pre-specified
Measure Title	Postoperative Drainage Volume Within 24 Hours After Study Drug Administration
Measure Description	The total volume of postoperative drainage from the surgical site over the 24 hours after study drug administration was recorded.
Time Frame	Up to 24 hours post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	Usual Care
Number of Participants Analyzed [units: participants]	**596**	**588**
Postoperative Drainage Volume Within 24 Hours After Study Drug Administration [units: mL] Mean (Standard Deviation)	**464 (367.5)**	**476 (375.3)**

Statistical Analysis 1 for Postoperative Drainage Volume Within 24 Hours After Study Drug Administration

Groups [1]	All groups
Method [2]	Generalized Linear Model
Mean Difference (Final Values) [3]	-7.2
95% Confidence Interval	-45.0 to 30.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Generalized Linear Model was adjusted for strata (renal function and use of prophylactic antithrombotic therapy) and investigational site.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Difference is Sugammadex versus Usual Care. A negative value indicates that the average adjusted drainage volume was lower in the sugammadex treatment group.

10. Other Pre-specified: Number of Participants Requiring Any Postoperative Transfusion [Time Frame: From end of study drug administration through approximately 120 hours after study drug administration]

Measure Type	Other Pre-specified
Measure Title	Number of Participants Requiring Any Postoperative Transfusion

Measure Description	The number of participants who received a transfusion unit (e.g., whole blood, packed RBCs, cell saver RBCs, fresh frozen plasma, platelets) that started after study drug administration and within 120 hours after study drug administration (or within 48 hours after any previous [i.e., predose] transfusion for participants who had received a previous transfusion) was determined.
Time Frame	From end of study drug administration through approximately 120 hours after study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants Requiring Any Postoperative Transfusion [units: participants]	**221**	**227**

Statistical Analysis 1 for Number of Participants Requiring Any Postoperative Transfusion

Groups [1]	All groups
Method [2]	Miettinen and Nurminen
Risk Difference (%) [3]	-2.7
95% Confidence Interval	-7.4 to 2.0

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Miettinen and Nurminen Method was adjusted for strata (renal function and use of prophylactic antithrombotic therapy) and investigational site
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Risk difference (%) = Sugammadex incidence - Usual Care incidence, adjusted for strata and investigational site

11. Other Pre-specified: Total Transfusion Volume in Participants Who Required Postoperative Transfusion [Time Frame: From end of study drug administration through approximately 120 hours after study drug administration]

Measure Type	Other Pre-specified
Measure Title	Total Transfusion Volume in Participants Who Required Postoperative Transfusion
Measure Description	Among participants who received a transfusion unit (e.g., whole blood, packed RBCs, cell saver RBCs, fresh frozen plasma, platelets) that started after study drug administration and within 120 hours after study drug administration (or within 48 hours after any previous [i.e., predose] transfusion for participants who had received a previous transfusion), the total volume of blood transfused post study drug was calculated. The volume of blood transfused post study drug (using linear interpolation when transfusions were ongoing at the time of study drug administration) was converted to grams of Hgb transfused, using RBC concentration information received from the investigators. The sum of Hgb transfused was standardized to “normal” volume Hgb in homologous whole blood, using 20 g/dL Hgb for calculation of the standardized volume.
Time Frame	From end of study drug administration through approximately 120 hours after study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Participants in APaT population who received a transfusion unit that started after study drug administration and within 120 hours after study drug administration (or within 48 hours after any previous [i.e., predose] transfusion for participants who had received a previous transfusion)

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**221**	**227**
Total Transfusion Volume in Participants Who Required Postoperative Transfusion [units: mL] Geometric Mean (Geometric Coefficient of Variation)	**335 (74%)**	**345 (84.5%)**

Statistical Analysis 1 for Total Transfusion Volume in Participants Who Required Postoperative Transfusion

Groups [1]	All groups

Method [2]	Generalized Linear Model
GMR [3]	1.10
95% Confidence Interval	0.98 to 1.24

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Generalized Linear Model was applied to transfusion volume transformed to the log-scale, adjusted for strata (renal function and use of prophylactic antithrombotic therapy) and investigational site. Result and 95% Confidence Interval was transformed back to the original scale.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	GMR is Sugammadex versus Usual Care

12. Other Pre-specified: Postoperative Changes in Hgb Concentrations Using the Bleeding Index [Time Frame: Baseline and Visit 3 (24-48 hours post study drug administration)]

Measure Type	Other Pre-specified
Measure Title	Postoperative Changes in Hgb Concentrations Using the Bleeding Index
Measure Description	The Bleeding Index was used to describe postoperative changes in Hgb concentrations at Visit 3. Bleeding Index = Hgb level at Visit 3 – Hgb level at baseline, adjusted for the amount of RBCs transfused. Missing baseline Hgb values were imputed using the overall mean Hgb value at baseline.
Time Frame	Baseline and Visit 3 (24-48 hours post study drug administration)
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	**Usual Care**
Number of Participants Analyzed [units: participants]	**596**	**588**

Postoperative Changes in Hgb Concentrations Using the Bleeding Index **[units: g/L]** **Mean (Standard Deviation)**	**-15.7 (15.7)**	**-17.4 (17.1)**

Statistical Analysis 1 for Postoperative Changes in Hgb Concentrations Using the Bleeding Index

Groups [1]	All groups
Method [2]	Generalized Linear Model
Mean Difference (Final Values) [3]	1.4
95% Confidence Interval	-0.4 to 3.1

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Generalized Linear Model was adjusted for strata (renal function and use of prophylactic antithrombotic therapy), investigational site and baseline hemoglobin value.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Difference is Sugammadex versus Usual Care. A positive value indicates that the average adjusted reduction in Hgb at Visit 3 (bleeding index) was lower in the sugammadex treatment group.

13. Other Pre-specified: Number of Participants With One or More Postoperative Anemia Adverse Events With Onset Within 72 Hours After Study Drug Administration [Time Frame: Up to 72 hours post study drug administration]

Measure Type	Other Pre-specified
Measure Title	Number of Participants With One or More Postoperative Anemia Adverse Events With Onset Within 72 Hours After Study Drug Administration
Measure Description	This measure is the incidence of postoperative anaemia with an onset within 72 hours after study drug administration. A participant is included in the count for this measure if an adverse event with any of the following event terms occurred in the participant with onset within the defined time frame: postoperative anaemia, anaemia, haemorrhagic anaemia, haemoglobin decreased or haemoglobin S decreased.
Time Frame	Up to 72 hours post study drug administration
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned

	to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Measured Values

	Sugammadex	Usual Care
Number of Participants Analyzed [units: participants]	**596**	**588**
Number of Participants With One or More Postoperative Anemia Adverse Events With Onset Within 72 Hours After Study Drug Administration [units: participants]	**124**	**132**

Statistical Analysis 1 for Number of Participants With One or More Postoperative Anemia Adverse Events With Onset Within 72 Hours After Study Drug Administration

Groups [1]	All groups
Method [2]	Miettinen and Nurminen
Risk Difference (%) [3]	-1.6
95% Confidence Interval	-6.3 to 3.1

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	No text entered.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Other relevant estimation information:
	Risk difference (%) = Sugammadex incidence - Usual Care incidence

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Up to 14 days post study drug administration
Additional Description	Adverse event tables include participants in APaT population

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned

	to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.
Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Serious Adverse Events

	Sugammadex	Usual Care
Total, serious adverse events		
# participants affected / at risk	**39/596 (6.54%)**	**40/588 (6.80%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**1/596 (0.17%)**	**1/588 (0.17%)**
# events	**1**	**1**
Cardiac disorders		
Acute myocardial infarction † 1		
# participants affected / at risk	**1/596 (0.17%)**	**1/588 (0.17%)**
# events	**1**	**1**
Mitral valve stenosis † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**
# events	**1**	**0**
Myocardial infarction † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Ventricular fibrillation † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Eye disorders		
Vitreous detachment † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Gastrointestinal disorders		
Colitis ischaemic † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**
# events	**1**	**0**
Diarrhoea † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**
# events	**1**	**0**
Subileus † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Tooth loss † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**

# events	1	0
General disorders		
Asthenia † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Device breakage † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Device dislocation † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Drug withdrawal syndrome † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Impaired healing † 1		
# participants affected / at risk	2/596 (0.34%)	4/588 (0.68%)
# events	2	4
Pain † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Infections and infestations		
Clostridial infection † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Nasopharyngitis † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Pneumonia † 1		
# participants affected / at risk	0/596 (0.00%)	2/588 (0.34%)
# events	0	2
Post procedural infection † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Rotavirus infection † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Sepsis † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Urinary tract infection † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Wound infection staphylococcal † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0

Injury, poisoning and procedural complications		
Anaemia postoperative † 1		
# participants affected / at risk	**0/596 (0.00%)**	**2/588 (0.34%)**
# events	**0**	**2**
Femoral nerve injury † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Femur fracture † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**
# events	**1**	**0**
Incision site haematoma † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Periprosthetic fracture † 1		
# participants affected / at risk	**1/596 (0.17%)**	**2/588 (0.34%)**
# events	**1**	**2**
Post procedural haemorrhage † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**
# events	**1**	**0**
Postoperative wound complication † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Seroma † 1		
# participants affected / at risk	**2/596 (0.34%)**	**1/588 (0.17%)**
# events	**2**	**1**
Subcutaneous haematoma † 1		
# participants affected / at risk	**2/596 (0.34%)**	**1/588 (0.17%)**
# events	**2**	**1**
Tendon rupture † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Wound dehiscence † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**
# events	**1**	**0**
Wound haemorrhage † 1		
# participants affected / at risk	**0/596 (0.00%)**	**1/588 (0.17%)**
# events	**0**	**1**
Wound secretion † 1		
# participants affected / at risk	**2/596 (0.34%)**	**4/588 (0.68%)**
# events	**2**	**4**
Investigations		
C-reactive protein increased † 1		
# participants affected / at risk	**1/596 (0.17%)**	**0/588 (0.00%)**
# events	**1**	**0**
Musculoskeletal and connective tissue disorders		

Groin pain † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Joint range of motion decreased † 1		
# participants affected / at risk	6/596 (1.01%)	1/588 (0.17%)
# events	6	1
Joint swelling † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Muscle haemorrhage † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Muscular weakness † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Osteonecrosis † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Chronic lymphocytic leukaemia † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Malignant melanoma † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Nervous system disorders		
Nerve compression † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Paraesthesia † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Peripheral nerve lesion † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Reversible ischaemic neurological deficit † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Transient ischaemic attack † 1		
# participants affected / at risk	1/596 (0.17%)	1/588 (0.17%)
# events	1	2
Renal and urinary disorders		
Oliguria † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)

# events	0	1
Renal failure † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Renal failure acute † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Respiratory, thoracic and mediastinal disorders		
Apnoea † 1		
# participants affected / at risk	0/596 (0.00%)	1/588 (0.17%)
# events	0	1
Pulmonary embolism † 1		
# participants affected / at risk	1/596 (0.17%)	1/588 (0.17%)
# events	1	1
Surgical and medical procedures		
Supportive care † 1		
# participants affected / at risk	1/596 (0.17%)	3/588 (0.51%)
# events	1	3
Vascular disorders		
Deep vein thrombosis † 1		
# participants affected / at risk	1/596 (0.17%)	0/588 (0.00%)
# events	1	0
Haematoma † 1		
# participants affected / at risk	3/596 (0.50%)	2/588 (0.34%)
# events	3	2

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 15.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Up to 14 days post study drug administration
Additional Description	Adverse event tables include participants in APaT population

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Sugammadex	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single intravenous (IV) administration of sugammadex 4 mg/kg and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of neostigmine/glycopyrrolate [or neostigmine/atropine] that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of sugammadex 4 mg/kg.

Usual Care	For participants in this Arm assigned to planned active reversal of neuromuscular blockade: single IV administration of neostigmine (up to a maximum dose of 5 mg) with glycopyrrolate or atropine and single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered). For participants in this Arm assigned to planned spontaneous recovery from neuromuscular blockade: single IV administration of placebo (normal saline [NaCl 0.9%] to match volume of sugammadex that would have been administered).

Other Adverse Events

	Sugammadex	Usual Care
Total, other (not including serious) adverse events		
# participants affected / at risk	**491/596 (82.38%)**	**499/588 (84.86%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**72/596 (12.08%)**	**74/588 (12.59%)**
# events	**75**	**74**
Gastrointestinal disorders		
Constipation † 1		
# participants affected / at risk	**128/596 (21.48%)**	**146/588 (24.83%)**
# events	**129**	**148**
Nausea † 1		
# participants affected / at risk	**124/596 (20.81%)**	**139/588 (23.64%)**
# events	**138**	**154**
Vomiting † 1		
# participants affected / at risk	**64/596 (10.74%)**	**70/588 (11.90%)**
# events	**67**	**74**
General disorders		
Oedema peripheral † 1		
# participants affected / at risk	**53/596 (8.89%)**	**47/588 (7.99%)**
# events	**55**	**50**
Pain † 1		
# participants affected / at risk	**91/596 (15.27%)**	**101/588 (17.18%)**
# events	**112**	**124**
Injury, poisoning and procedural complications		
Anaemia postoperative † 1		
# participants affected / at risk	**63/596 (10.57%)**	**65/588 (11.05%)**
# events	**64**	**66**
Procedural pain † 1		
# participants affected / at risk	**203/596 (34.06%)**	**234/588 (39.80%)**
# events	**224**	**259**
Metabolism and nutrition disorders		
Hypokalaemia † 1		
# participants affected / at risk	**33/596 (5.54%)**	**45/588 (7.65%)**
# events	**33**	**47**
Musculoskeletal and connective tissue disorders		

Arthralgia † 1		
# participants affected / at risk	**54/596 (9.06%)**	**40/588 (6.80%)**
# events	**84**	**60**
Psychiatric disorders		
Insomnia † 1		
# participants affected / at risk	**50/596 (8.39%)**	**54/588 (9.18%)**
# events	**50**	**55**
Sleep disorder † 1		
# participants affected / at risk	**87/596 (14.60%)**	**84/588 (14.29%)**
# events	**90**	**86**
Skin and subcutaneous tissue disorders		
Erythema † 1		
# participants affected / at risk	**26/596 (4.36%)**	**32/588 (5.44%)**
# events	**31**	**38**
Vascular disorders		
Haematoma † 1		
# participants affected / at risk	**59/596 (9.90%)**	**53/588 (9.01%)**
# events	**61**	**54**
Hypotension † 1		
# participants affected / at risk	**27/596 (4.53%)**	**37/588 (6.29%)**
# events	**28**	**40**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 15.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** Initial public presentation of the Investigator's results will occur only together with the other sites unless permission is obtained from Sponsor. Sponsor must be able to review all proposed results communications regarding study 45 days prior to submission for publication/presentation. In case of disagreement concerning appropriateness of materials, Investigator and Sponsor must meet to make a good faith effort to discuss/resolve the issues, prior to submission for publication/presentation.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
phone: 1-800-672-6372
e-mail: ClinicalTrialsDisclosure@merck.com

No publications provided

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT01422304 History of Changes
Other Study ID Numbers:	P07038 2011-001201-27 (EudraCT Number) MK-8616-059 (Other Identifier: Merck protocol number)
Study First Received:	August 22, 2011
Results First Received:	August 19, 2013
Last Updated:	September 3, 2015
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices

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