Comparing 4.0 mg.Kg-1 Sugammadex With Placebo in the Reversal of Profound Neuromuscular Blockade (P05767)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

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

ClinicalTrials.gov Identifier:
NCT00758485

First received: September 23, 2008
Last updated: August 4, 2015
Last verified: August 2015
History of Changes

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Purpose

The current trial was designed to demonstrate faster recovery in participants undergoing elective surgeries requiring profound neuromuscular blockade induced by rocuronium to a fourth twitch/first twitch (T4/T1) ratio of 0.9, after reversal of a target depth of neuromuscular blockade (NMB) of 1-2 Post Tetanic Count (PTC) by 4.0 mg.kg-1 Sugammadex compared to Placebo, to evaluate the safety of 4.0 mg.kg-1 Sugammadex and to evaluate the Operating Room (OR) and Post Anesthetic Care Unit (PACU) length of stay for these participants.

Condition	Intervention	Phase
Anesthesia Neuromuscular Blockade	Drug: Sugammadex Drug: 0.9% sodium chloride (NaCl)	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Single Blind (Outcomes Assessor)
Primary Purpose: Treatment

Official Title: A Randomized, Safety-assessor Blinded Trial Comparing 4.0 mg.Kg-1 Sugammadex With Placebo in Adult Subjects Scheduled for Surgery Requiring Profound Neuromuscular Blockade

Resource links provided by NLM:

Drug Information available for: Sugammadex Sugammadex sodium

U.S. FDA Resources

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

Primary Outcome Measures:

- Time From Start of Administration of Investigational Medicinal Product (IMP, Sugammadex or Placebo) to Recovery of the Fourth Twitch/First Twitch (T4/T1) Ratio to 0.9 [Time Frame: From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.9 (estimated from ~2 minutes up to ~90 minutes)] [Designated as safety issue: No]

  Neuromuscular functioning was monitored by applying repetitive Train-Of-Four (TOF) electrical stimulations to the ulnar nerve every 15 seconds & assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to the magnitudes (height) of the first and fourth twitches, respectively, after TOF nerve stimulation. The T4/T1 Ratio (a percentage that is expressed as a decimal of up to 1.0) indicates the extent of recovery from neuromuscular blockade (NMB), with a higher ratio indicating a greater recovery from NMB. In this study, twitch responses were recorded until the T4/T1 Ratio reached >=0.9, the minimum acceptable ratio that indicated complete recovery from NMB. A shorter time to recovery of the T4/T1 Ratio >=0.9 indicates a faster recovery from NMB.

Secondary Outcome Measures:

- Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.7 [Time Frame: From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.7 (estimated from ~1 minute up to ~70 minutes)] [Designated as safety issue: No]

  Neuromuscular functioning was monitored by applying repetitive TOF electrical stimulations to the ulnar nerve every 15 seconds & assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to the magnitudes (height) of the first and fourth twitches, respectively, after TOF nerve stimulation. The T4/T1 Ratio (a percentage that is expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB, with a higher ratio indicating a greater recovery from NMB.

- Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.8 [Time Frame: From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.8 (estimated from ~2 minutes up to ~80 minutes)] [Designated as safety issue: No]

  Neuromuscular functioning was monitored by applying repetitive TOF electrical stimulations to the ulnar nerve every 15 seconds & assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to the magnitudes (height) of the first and fourth twitches, respectively, after TOF nerve stimulation. The T4/T1 Ratio (a percentage that is expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB, with a higher ratio indicating a greater recovery from NMB.

Enrollment:	140
Study Start Date:	October 2008
Study Completion Date:	June 2009
Primary Completion Date:	May 2009 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: sugammadex Participants receiving 4.0 mg.kg-1 Sugammadex at a target depth of NMB of 1-2 PTC after the last dose of rocuronium	Drug: Sugammadex At a target depth of NMB of 1-2 PTC after the last dose of rocuronium, a bolus dose of 4.0 mg.kg-1 sugammadex (volume based on the actual body weight of the participant) will be administered, within 10 seconds into a fast running venous infusion. Other Names: • Org 25969 • SCH 900616 • MK-8616 • Bridion®
Placebo Comparator: Placebo Participants receiving Placebo (0.9% NaCl) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium	Drug: 0.9% sodium chloride (NaCl) At a target depth of NMB of 1-2 PTC after the last dose of rocuronium, a bolus dose of placebo (0.9% NaCl, volume based on the actual body weight of the participant) will be administered, within 10 seconds into a fast running venous infusion. Other Name: Placebo

Eligibility

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

Criteria

Inclusion Criteria:

- Male or female participants
- American Society of Anesthesiologists (ASA) class 1, 2 or 3
- Age >=18 years
- Scheduled to undergo a surgery requiring profound NMB such as cardiovascular, gynaecologic, neurologic and thoracic surgical procedures under general anesthesia requiring neuromuscular relaxation with rocuronium for endotracheal intubation and if applicable maintenance of NMB in a position allowing neuromuscular monitoring
- Given written informed consent

Exclusion Criteria:

- Participants known or suspected to have neuromuscular disorders affecting NMB

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

Publications:

Rahe-Meyer N, Berger C, Wittmann M, Solomon C, Abels EA, Rietbergen H, Reuter DA. Recovery from prolonged deep rocuronium-induced neuromuscular blockade: A randomized comparison of sugammadex reversal with spontaneous recovery. Anaesthesist. 2015 Jul;64(7):506-12. doi: 10.1007/s00101-015-0048-0. Epub 2015 Jul 1.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00758485 History of Changes
Other Study ID Numbers:	P05767 2008-002518-23 19.4.316 MK-8616-004
Study First Received:	September 23, 2008
Results First Received:	March 11, 2013
Last Updated:	August 4, 2015
Health Authority:	Germany: Federal Institute for Drugs and Medical Devices

ClinicalTrials.gov processed this record on April 10, 2016

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ClinicalTrials.gov Identifier:
NCT00758485

First received: September 23, 2008
Last updated: August 4, 2015
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History of Changes

Results First Received: March 11, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Parallel Assignment; Masking: Single Blind (Outcomes Assessor); Primary Purpose: Treatment
Conditions:	Anesthesia Neuromuscular Blockade
Interventions:	Drug: Sugammadex Drug: 0.9% sodium chloride (NaCl)

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
Participants were recruited from 10 sites in Germany from November 2008 to May 2009.

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	Participants receiving 4.0 mg.kg-1 Sugammadex at a target depth of neuromuscular blockade (NMB) of 1-2 Post Tetanic Count (PTC) after the last dose of rocuronium
Placebo	Participants receiving Placebo (0.9% sodium chloride[NaCl]) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium

Participant Flow: Overall Study

	Sugammadex	Placebo
STARTED	**70**	**70**
TREATED	**69**	**68**
COMPLETED	**69**	**67**
NOT COMPLETED	**1**	**3**
Lost to Follow-up	**0**	**1**
Not Treated	**1**	**2**

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	Participants receiving 4.0 mg.kg-1 Sugammadex at a target depth of NMB of 1-2 PTC after the last dose of rocuronium.
Placebo	Participants receiving Placebo (0.9% NaCl) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium.
Total	Total of all reporting groups

Baseline Measures

	Sugammadex	Placebo	Total
Number of Participants [units: participants]	**69**	**68**	**137**
Age [units: years] Mean (Standard Deviation)	**57 (17)**	**57 (14)**	**57 (16)**
Gender [units: participants]			
Female	**21**	**25**	**46**
Male	**48**	**43**	**91**

Outcome Measures

Hide All Outcome Measures

1. Primary: Time From Start of Administration of Investigational Medicinal Product (IMP, Sugammadex or Placebo) to Recovery of the Fourth Twitch/First Twitch (T4/T1) Ratio to 0.9 [Time Frame: From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.9 (estimated from ~2 minutes up to ~90 minutes)]

Measure Type	Primary
Measure Title	Time From Start of Administration of Investigational Medicinal Product (IMP, Sugammadex or Placebo) to Recovery of the Fourth Twitch/First Twitch (T4/T1) Ratio to 0.9
Measure Description	Neuromuscular functioning was monitored by applying repetitive Train-Of-Four (TOF) electrical stimulations to the ulnar nerve every 15 seconds & assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to the magnitudes (height) of the first and fourth twitches, respectively, after TOF nerve stimulation. The T4/T1 Ratio (a percentage that is expressed as a decimal of up to 1.0) indicates the extent of recovery from neuromuscular blockade (NMB), with a higher ratio indicating a greater recovery from NMB. In this study, twitch responses were recorded until the T4/T1 Ratio reached >=0.9, the minimum acceptable ratio that indicated complete recovery from NMB. A shorter time to recovery of the T4/T1 Ratio >=0.9 indicates a faster recovery from NMB.
Time Frame	From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.9 (estimated from ~2 minutes up to ~90 minutes)
Safety Issue	No

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.
The Intent-to-Treat (ITT) Population consisted of all participants who received either Sugammadex or Placebo and had at least one efficacy measurement. Imputed recovery times were used in cases of missing times.

Reporting Groups

	Description
Sugammadex	Participants receiving 4.0 mg/kg-1 Sugammadex at a target depth of NMB of 1-2 Post Tetanic Count (PTC) after the last dose of rocuronium
Placebo	Participants receiving Placebo (0.9% NaCl) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium

Measured Values

	Sugammadex	**Placebo**
Number of Participants Analyzed [units: participants]	**69**	**65**
Time From Start of Administration of Investigational Medicinal Product (IMP, Sugammadex or Placebo) to Recovery of the Fourth Twitch/First Twitch (T4/T1) Ratio to 0.9 [units: minutes] Geometric Mean (95% Confidence Interval)	**2.2 (1.9 to 2.5)**	**89.8 (80.1 to 100.7)**

No statistical analysis provided for Time From Start of Administration of Investigational Medicinal Product (IMP, Sugammadex or Placebo) to Recovery of the Fourth Twitch/First Twitch (T4/T1) Ratio to 0.9

2. Secondary: Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.7 [Time Frame: From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.7 (estimated from ~1 minute up to ~70 minutes)]

Measure Type	Secondary
Measure Title	Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.7
Measure Description	Neuromuscular functioning was monitored by applying repetitive TOF electrical stimulations to the ulnar nerve every 15 seconds & assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to the magnitudes (height) of the first and fourth twitches, respectively, after TOF nerve stimulation. The T4/T1 Ratio (a percentage that is expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB, with a higher ratio indicating a greater recovery from NMB.
Time Frame	From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.7 (estimated from ~1 minute up to ~70 minutes)
Safety Issue	No

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.
The ITT Population consisted of all participants who received either Sugammadex or Placebo and had at least one efficacy measurement. Imputed recovery times were used in cases of missing times.

Reporting Groups

	Description
Sugammadex	Participants receiving 4.0 mg.kg-1 Sugammadex at a target depth of NMB of 1-2 PTC after the last dose of rocuronium
Placebo	Participants receiving Placebo (0.9% NaCl) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium

Measured Values

	Sugammadex	**Placebo**
Number of Participants Analyzed [units: participants]	**69**	**65**
Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.7 [units: minutes] Geometric Mean (95% Confidence Interval)	**1.6 (1.4 to 1.8)**	**70.1 (62.7 to 78.4)**

No statistical analysis provided for Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.7

3. Secondary: Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.8 [Time Frame: From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.8 (estimated from ~2 minutes up to ~80 minutes)]

Measure Type	Secondary
Measure Title	Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.8
Measure Description	Neuromuscular functioning was monitored by applying repetitive TOF electrical stimulations to the ulnar nerve every 15 seconds & assessing twitch response at the adductor pollicis muscle. T1 and T4 refer to the magnitudes (height) of the first and fourth twitches, respectively, after TOF nerve stimulation. The T4/T1 Ratio (a percentage that is expressed as a decimal of up to 1.0) indicates the extent of recovery from NMB, with a higher ratio indicating a greater recovery from NMB.
Time Frame	From Start of IMP Administration to Recovery of the T4/T1 Ratio to 0.8 (estimated from ~2 minutes up to ~80 minutes)

Safety Issue	No

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.
The ITT Population consisted of all participants who received either Sugammadex or Placebo and had at least one efficacy measurement. Imputed recovery times were used in cases of missing times.

Reporting Groups

	Description
Sugammadex	Participants receiving 4.0 mg.kg-1 Sugammadex at a target depth of NMB of 1-2 PTC after the last dose of rocuronium
Placebo	Participants receiving Placebo (0.9% NaCl) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium

Measured Values

	Sugammadex	Placebo
Number of Participants Analyzed [units: participants]	**69**	**65**
Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.8 [units: minutes] Geometric Mean (95% Confidence Interval)	**1.8 (1.6 to 2.0)**	**78.8 (70.2 to 88.5)**

No statistical analysis provided for Time From Start of Administration of IMP to Recovery of the T4/T1 Ratio to 0.8

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Up to 7 days after administration of IMP
Additional Description	The All Subjects Treated Population consisted of all randomized participants who received IMP.

Reporting Groups

	Description
Sugammadex	Participants receiving 4.0 mg.kg-1 Sugammadex at a target depth of NMB of 1-2 PTC after the last dose of rocuronium
Placebo	Participants receiving Placebo (0.9% NaCl) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium

Serious Adverse Events

	Sugammadex	Placebo
Total, serious adverse events		
# participants affected / at risk	**4/69 (5.80%)**	**4/68 (5.88%)**
Gastrointestinal disorders		

Diverticular Perforation [1]		
# participants affected / at risk	**0/69 (0.00%)**	**1/68 (1.47%)**
# events	**0**	**1**
Injury, poisoning and procedural complications		
Post Procedural Complication [1]		
# participants affected / at risk	**1/69 (1.45%)**	**1/68 (1.47%)**
# events	**1**	**1**
Post Procedural Haemorrhage [1]		
# participants affected / at risk	**1/69 (1.45%)**	**1/68 (1.47%)**
# events	**1**	**1**
Skin Laceration [1]		
# participants affected / at risk	**0/69 (0.00%)**	**1/68 (1.47%)**
# events	**0**	**1**
Psychiatric disorders		
Alcohol Withdrawal Syndrome [1]		
# participants affected / at risk	**1/69 (1.45%)**	**0/68 (0.00%)**
# events	**1**	**0**
Vascular disorders		
Lymphocele [1]		
# participants affected / at risk	**1/69 (1.45%)**	**0/68 (0.00%)**
# events	**1**	**0**

1 Term from vocabulary, MedDRA (12.1)

Other Adverse Events

Hide Other Adverse Events

Time Frame	Up to 7 days after administration of IMP
Additional Description	The All Subjects Treated Population consisted of all randomized participants who received IMP.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Sugammadex	Participants receiving 4.0 mg.kg-1 Sugammadex at a target depth of NMB of 1-2 PTC after the last dose of rocuronium
Placebo	Participants receiving Placebo (0.9% NaCl) at a target depth of NMB of 1-2 PTC after the last dose of rocuronium

Other Adverse Events

	Sugammadex	**Placebo**
Total, other (not including serious) adverse events		

# participants affected / at risk	44/69 (63.77%)	48/68 (70.59%)
Gastrointestinal disorders		
Constipation [1]		
# participants affected / at risk	6/69 (8.70%)	4/68 (5.88%)
# events	6	4
Flatulence [1]		
# participants affected / at risk	4/69 (5.80%)	7/68 (10.29%)
# events	4	7
Nausea [1]		
# participants affected / at risk	9/69 (13.04%)	11/68 (16.18%)
# events	9	12
Vomiting [1]		
# participants affected / at risk	5/69 (7.25%)	5/68 (7.35%)
# events	5	5
General disorders		
Pyrexia [1]		
# participants affected / at risk	4/69 (5.80%)	4/68 (5.88%)
# events	4	4
Injury, poisoning and procedural complications		
Procedural Nausea [1]		
# participants affected / at risk	3/69 (4.35%)	4/68 (5.88%)
# events	3	4
Procedural Pain [1]		
# participants affected / at risk	29/69 (42.03%)	32/68 (47.06%)
# events	30	33
Wound Complication [1]		
# participants affected / at risk	11/69 (15.94%)	10/68 (14.71%)
# events	13	10
Nervous system disorders		
Dizziness [1]		
# participants affected / at risk	1/69 (1.45%)	5/68 (7.35%)
# events	1	5
Headache [1]		
# participants affected / at risk	7/69 (10.14%)	5/68 (7.35%)
# events	7	5
Psychiatric disorders		
Sleep Disorder [1]		
# participants affected / at risk	4/69 (5.80%)	4/68 (5.88%)
# events	4	4

1 Term from vocabulary, MedDRA (12.1)

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 **NOT** 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.

Results Point of Contact:

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

Publications of Results:

Rahe-Meyer N, Berger C, Wittmann M, Solomon C, Abels EA, Rietbergen H, Reuter DA. Recovery from prolonged deep rocuronium-induced neuromuscular blockade: A randomized comparison of sugammadex reversal with spontaneous recovery. Anaesthesist. 2015 Jul;64(7):506-12. doi: 10.1007/s00101-015-0048-0. Epub 2015 Jul 1.

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Other Study ID Numbers:	P05767 2008-002518-23 (EudraCT Number) 19.4.316 (Other Identifier: Organon Protocol ID) MK-8616-004 (Other Identifier: Merck Protocol ID)
Study First Received:	September 23, 2008
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