

**Clinical trial results:****A Randomized, Assessor-blind, Dose-ranging, Phase IIIB, Multicenter Trial Comparing the Intubating Conditions and Time Course of Block of Three Different Intubating Doses (0.45 mg/kg, 0.6 mg/kg, and 1.0 mg/kg) of Zemuron® in Pediatric and Adolescent Subjects Under General Anesthesia****Summary**

EudraCT number	2005-002928-34
Trial protocol	BE Outside EU/EEA
Global end of trial date	26 July 2007

Results information

Result version number	v1
This version publication date	17 March 2016
First version publication date	17 March 2016

Trial information**Trial identification**

Sponsor protocol code	P05798
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00124722
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Registration number: MK-8085-002, Organon Registration number: 021049

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 July 2007
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 July 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of this study is to evaluate the time course of muscle relaxation after administration of three different single intravenous (IV) bolus doses of Zemuron (rocuronium bromide) for intubation (insertion of a tube through the nose or mouth into the trachea to provide artificial ventilation) in term neonates (birth to <28 days old), infants (28 days to ≤3 months), toddlers (>3 months to ≤2 years), children (>2 years to ≤11 years of age) and adolescents (>11 years to ≤17 years of age). Participants in each of the age groups will be randomized to one of 3 Zemuron doses: 0.45 mg/kg, 0.6 mg/kg, or 1.0 mg/kg.

Protection of trial subjects:

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

Background therapy:

Sevoflurane at 2.0-2.5 minimum alveolar concentration (MAC) to up to 7%-8% inspired concentration in nitrous oxide at 0%-70%, or propofol 1-3 mg/kg (may be used in neonates only) for induction of anesthesia; isoflurane 1.0±0.2% expired end-tidal concentration in 0%-70% nitrous oxide and, if needed, propofol as intermittent bolus dose(s) (0.5-2 mg/kg) or infusion (50-150 µg/kg/min) for maintenance of anesthesia.

Evidence for comparator: -

Actual start date of recruitment	16 December 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 196
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	207
EEA total number of subjects	11

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	18
Infants and toddlers (28 days-23 months)	77
Children (2-11 years)	57
Adolescents (12-17 years)	55
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 207 participants were enrolled and randomized in the trial; of these 189 received study drug. Allocation of participants to age groups "children" and "adolescent" in Trial Information versus other sections (including Disposition) differ slightly due to differences in age range definitions used (i.e., EudraCT versus protocol definitions).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor ^[1]

Blinding implementation details:

The assessor of the intubation conditions will be blinded to the study drug treatment, and will not be the person administering the study drug.

Arms

Are arms mutually exclusive?	Yes
Arm title	Zemuron 0.45 mg/kg – Neonates

Arm description:

Neonate participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV bolus administered prior to intubation

Arm title	Zemuron 0.6 mg/kg – Neonates
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Arm description:

Neonate participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV bolus administered prior to intubation

Arm title	Zemuron 1.0 mg/kg – Neonates
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Arm description:

Neonate participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Arm type	Experimental
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Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.45 mg/kg – Infants
Arm description:	
Infant participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.6 mg/kg – Infants
Arm description:	
Infant participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 1.0 mg/kg – Infants
Arm description:	
Infant participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.45 mg/kg – Toddlers
Arm description:	
Toddler participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Arm type	Experimental

Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.6 mg/kg – Toddlers
Arm description:	
Toddler participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 1.0 mg/kg – Toddlers
Arm description:	
Toddler participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.45 mg/kg – Children
Arm description:	
Child participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.6 mg/kg – Children
Arm description:	
Child participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Arm type	Experimental

Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 1.0 mg/kg – Children
Arm description:	
Child participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.45 mg/kg – Adolescents
Arm description:	
Adolescent participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 0.6 mg/kg – Adolescents
Arm description:	
Adolescent participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Arm type	Experimental
Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Single IV bolus administered prior to intubation	
Arm title	Zemuron 1.0 mg/kg – Adolescents
Arm description:	
Adolescent participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Arm type	Experimental

Investigational medicinal product name	Zemuron
Investigational medicinal product code	
Other name	Esmeron, rocuronium bromide, MK-8085, SCH 900085, Org 9426
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV bolus administered prior to intubation

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The only role blinded in this study was assessor of the intubation conditions.

Number of subjects in period 1	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates
Started	5	7	6
Treated	5	7	6
Completed	5	7	5
Not completed	0	0	1
Adverse event, non-fatal	-	-	-
Inadvertently discontinued	-	-	-
Surgery was complete	-	-	1
Protocol deviation	-	-	-
Not treated	-	-	-

Number of subjects in period 1	Zemuron 0.45 mg/kg – Infants	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants
Started	9	8	5
Treated	9	6	5
Completed	8	6	5
Not completed	1	2	0
Adverse event, non-fatal	-	-	-
Inadvertently discontinued	-	-	-
Surgery was complete	-	-	-
Protocol deviation	1	-	-
Not treated	-	2	-

Number of subjects in period 1	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers	Zemuron 1.0 mg/kg – Toddlers
Started	18	20	17
Treated	18	16	15
Completed	17	16	15
Not completed	1	4	2
Adverse event, non-fatal	-	-	-
Inadvertently discontinued	1	-	-
Surgery was complete	-	-	-
Protocol deviation	-	-	-
Not treated	-	4	2

Number of subjects in period 1	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Started	17	21	17
Treated	16	21	16
Completed	15	21	16
Not completed	2	0	1
Adverse event, non-fatal	1	-	-
Inadvertently discontinued	-	-	-
Surgery was complete	-	-	-
Protocol deviation	-	-	-
Not treated	1	-	1

Number of subjects in period 1	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents
Started	20	17	20
Treated	18	16	15
Completed	18	16	15
Not completed	2	1	5
Adverse event, non-fatal	-	-	-
Inadvertently discontinued	-	-	-
Surgery was complete	-	-	-
Protocol deviation	-	-	-
Not treated	2	1	5

Baseline characteristics

Reporting groups

Reporting group title	Zemuron 0.45 mg/kg – Neonates
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Reporting group description:

Neonate participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Reporting group title	Zemuron 0.6 mg/kg – Neonates
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Reporting group description:

Neonate participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Reporting group title	Zemuron 1.0 mg/kg – Neonates
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Reporting group description:

Neonate participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Reporting group title	Zemuron 0.45 mg/kg – Infants
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Reporting group description:

Infant participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Reporting group title	Zemuron 0.6 mg/kg – Infants
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Reporting group description:

Infant participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Reporting group title	Zemuron 1.0 mg/kg – Infants
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Reporting group description:

Infant participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Reporting group title	Zemuron 0.45 mg/kg – Toddlers
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Reporting group description:

Toddler participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Reporting group title	Zemuron 0.6 mg/kg – Toddlers
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Reporting group description:

Toddler participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Reporting group title	Zemuron 1.0 mg/kg – Toddlers
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Reporting group description:

Toddler participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Reporting group title	Zemuron 0.45 mg/kg – Children
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Reporting group description:

Child participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Reporting group title	Zemuron 0.6 mg/kg – Children
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Reporting group description:

Child participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Reporting group title	Zemuron 1.0 mg/kg – Children
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Reporting group description:

Child participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Reporting group title	Zemuron 0.45 mg/kg – Adolescents
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Reporting group description:

Adolescent participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Reporting group title	Zemuron 0.6 mg/kg – Adolescents
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Reporting group description:

Adolescent participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Reporting group title	Zemuron 1.0 mg/kg – Adolescents
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Reporting group description:

Adolescent participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Reporting group values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates
Number of subjects	5	7	6
Age Categorical Units: Subjects			
≤18 years	5	7	6
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	1	1	1
Male	4	6	5

Reporting group values	Zemuron 0.45 mg/kg – Infants	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants
Number of subjects	9	8	5
Age Categorical Units: Subjects			
≤18 years	9	8	5
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	4	2	2
Male	5	6	3

Reporting group values	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers	Zemuron 1.0 mg/kg – Toddlers
Number of subjects	18	20	17
Age Categorical Units: Subjects			
≤18 years	18	20	17
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	5	3	7
Male	13	17	10

Reporting group values	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Number of subjects	17	21	17
Age Categorical Units: Subjects			
≤18 years	17	21	17
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	7	14	8
Male	10	7	9

Reporting group values	Zemuron 0.45 mg/kg –	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents

Adolescents

Number of subjects	20	17	20
Age Categorical Units: Subjects			
≤18 years	20	17	20
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	7	8	8
Male	13	9	12

Reporting group values	Total		
Number of subjects	207		
Age Categorical Units: Subjects			
≤18 years	207		
Between 18 and 65 years	0		
≥65 years	0		
Gender Categorical Units: Subjects			
Female	78		
Male	129		

Subject analysis sets

Subject analysis set title	Zemuron 0.45 mg/kg – Neonates
Subject analysis set type	Full analysis
Subject analysis set description: Neonate participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.6 mg/kg – Neonates
Subject analysis set type	Full analysis
Subject analysis set description: Neonate participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Subject analysis set title	Zemuron 1.0 mg/kg – Neonates
Subject analysis set type	Full analysis
Subject analysis set description: Neonate participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.45 mg/kg – Infants
Subject analysis set type	Full analysis
Subject analysis set description: Infant participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.6 mg/kg – Infants
Subject analysis set type	Full analysis
Subject analysis set description: Infant participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Subject analysis set title	Zemuron 1.0 mg/kg – Infants
Subject analysis set type	Full analysis
Subject analysis set description: Infant participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.45 mg/kg – Toddlers

Subject analysis set type	Full analysis
Subject analysis set description: Toddler participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.6 mg/kg – Toddlers
Subject analysis set type	Full analysis
Subject analysis set description: Toddler participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Subject analysis set title	Zemuron 1.0 mg/kg – Toddlers
Subject analysis set type	Full analysis
Subject analysis set description: Toddler participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.45 mg/kg – Children
Subject analysis set type	Full analysis
Subject analysis set description: Child participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.6 mg/kg – Children
Subject analysis set type	Full analysis
Subject analysis set description: Child participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Subject analysis set title	Zemuron 1.0 mg/kg – Children
Subject analysis set type	Full analysis
Subject analysis set description: Child participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.45 mg/kg – Adolescents
Subject analysis set type	Full analysis
Subject analysis set description: Adolescent participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron	
Subject analysis set title	Zemuron 0.6 mg/kg – Adolescents
Subject analysis set type	Full analysis
Subject analysis set description: Adolescent participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron	
Subject analysis set title	Zemuron 1.0 mg/kg – Adolescents
Subject analysis set type	Full analysis
Subject analysis set description: Adolescent participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron	

Reporting group values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates
Number of subjects	5	7	6
Age Categorical Units: Subjects			
≤18 years	5	7	6
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	1	1	1
Male	4	6	5

Reporting group values	Zemuron 0.45 mg/kg – Infants	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants
Number of subjects	9	6	5

Age Categorical Units: Subjects			
≤18 years	9	6	5
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	4	0	2
Male	5	6	3

Reporting group values	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers	Zemuron 1.0 mg/kg – Toddlers
Number of subjects	18	16	15
Age Categorical Units: Subjects			
≤18 years	18	16	15
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	5	3	6
Male	13	13	9

Reporting group values	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Number of subjects	16	21	16
Age Categorical Units: Subjects			
≤18 years	16	21	16
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	6	14	7
Male	10	7	9

Reporting group values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents
Number of subjects	18	16	15
Age Categorical Units: Subjects			
≤18 years	18	16	15
Between 18 and 65 years	0	0	0
≥65 years	0	0	0
Gender Categorical Units: Subjects			
Female	7	7	7
Male	11	9	8

End points

End points reporting groups

Reporting group title	Zemuron 0.45 mg/kg – Neonates
Reporting group description:	Neonate participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron
Reporting group title	Zemuron 0.6 mg/kg – Neonates
Reporting group description:	Neonate participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron
Reporting group title	Zemuron 1.0 mg/kg – Neonates
Reporting group description:	Neonate participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron
Reporting group title	Zemuron 0.45 mg/kg – Infants
Reporting group description:	Infant participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron
Reporting group title	Zemuron 0.6 mg/kg – Infants
Reporting group description:	Infant participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron
Reporting group title	Zemuron 1.0 mg/kg – Infants
Reporting group description:	Infant participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron
Reporting group title	Zemuron 0.45 mg/kg – Toddlers
Reporting group description:	Toddler participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron
Reporting group title	Zemuron 0.6 mg/kg – Toddlers
Reporting group description:	Toddler participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron
Reporting group title	Zemuron 1.0 mg/kg – Toddlers
Reporting group description:	Toddler participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron
Reporting group title	Zemuron 0.45 mg/kg – Children
Reporting group description:	Child participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron
Reporting group title	Zemuron 0.6 mg/kg – Children
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Reporting group description:	Child participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron
Reporting group title	Zemuron 0.45 mg/kg – Adolescents
Reporting group description:	Adolescent participants randomized to receive a single IV bolus intubation dose of 0.45 mg/kg Zemuron
Reporting group title	Zemuron 0.6 mg/kg – Adolescents
Reporting group description:	Adolescent participants randomized to receive a single IV bolus intubation dose of 0.6 mg/kg Zemuron
Reporting group title	Zemuron 1.0 mg/kg – Adolescents
Reporting group description:	Adolescent participants randomized to receive a single IV bolus intubation dose of 1.0 mg/kg Zemuron
Subject analysis set title	Zemuron 0.45 mg/kg – Neonates
Subject analysis set type	Full analysis

Subject analysis set description:

Neonate participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Subject analysis set title	Zemuron 0.6 mg/kg – Neonates
Subject analysis set type	Full analysis

Subject analysis set description:

Neonate participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Subject analysis set title	Zemuron 1.0 mg/kg – Neonates
Subject analysis set type	Full analysis

Subject analysis set description:

Neonate participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Subject analysis set title	Zemuron 0.45 mg/kg – Infants
Subject analysis set type	Full analysis

Subject analysis set description:

Infant participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Subject analysis set title	Zemuron 0.6 mg/kg – Infants
Subject analysis set type	Full analysis

Subject analysis set description:

Infant participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Subject analysis set title	Zemuron 1.0 mg/kg – Infants
Subject analysis set type	Full analysis

Subject analysis set description:

Infant participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Subject analysis set title	Zemuron 0.45 mg/kg – Toddlers
Subject analysis set type	Full analysis

Subject analysis set description:

Toddler participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Subject analysis set title	Zemuron 0.6 mg/kg – Toddlers
Subject analysis set type	Full analysis

Subject analysis set description:

Toddler participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Subject analysis set title	Zemuron 1.0 mg/kg – Toddlers
Subject analysis set type	Full analysis

Subject analysis set description:

Toddler participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Subject analysis set title	Zemuron 0.45 mg/kg – Children
Subject analysis set type	Full analysis

Subject analysis set description:

Child participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Subject analysis set title	Zemuron 0.6 mg/kg – Children
Subject analysis set type	Full analysis

Subject analysis set description:

Child participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Subject analysis set title	Zemuron 1.0 mg/kg – Children
Subject analysis set type	Full analysis

Subject analysis set description:

Child participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Subject analysis set title	Zemuron 0.45 mg/kg – Adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Adolescent participants who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Subject analysis set title	Zemuron 0.6 mg/kg – Adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Adolescent participants who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Subject analysis set title	Zemuron 1.0 mg/kg – Adolescents
Subject analysis set type	Full analysis

Subject analysis set description:

Adolescent participants who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Primary: Time from End of Zemuron Intubating Dose to Reappearance of T3 (the third twitch of a Train of Four [TOF] stimulation)

End point title	Time from End of Zemuron Intubating Dose to Reappearance of T3 (the third twitch of a Train of Four [TOF] stimulation)
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End point description:

The duration from end of administration of the Zemuron intubating dose to reappearance of T3 was measured. Analysis population is the Per Protocol group, which is all participants who were randomized after protocol Amendment 2 (major revision to study), received study drug, had at least one efficacy parameter measured and did not have any major protocol violations. Also to be included, participant must have an evaluable assessment for this measure.

End point type	Primary
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End point timeframe:

From end of administration of Zemuron intubating dose to reappearance of T3

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	6	2	8
Units: minutes				
arithmetic mean (standard deviation)	49.53 (± 11.64)	55.68 (± 32.31)	114.43 (± 30.91)	46.44 (± 23.07)

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	3	15	14
Units: minutes				
arithmetic mean (standard deviation)	62.34 (± 20.36)	116.48 (± 34.23)	35.3 (± 11.26)	41.77 (± 11.6)

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	20	14
Units: minutes				
arithmetic mean (standard deviation)	76.07 (± 23.57)	23.55 (± 5.16)	38.27 (± 11.57)	53.46 (± 16.13)

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	11	
Units: minutes				
arithmetic mean (standard deviation)	36.96 (± 13.39)	41.78 (± 15.22)	61.56 (± 19.4)	

Statistical analyses

Statistical analysis title	Treatment Comparison by Age Group
Statistical analysis description:	
Two-way analysis of variance (ANOVA) model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 0.6 mg group	
Comparison groups	Zemuron 0.45 mg/kg – Neonates v Zemuron 0.6 mg/kg – Neonates
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4692
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-19.711111
Confidence interval	
level	95 %
sides	2-sided
lower limit	-88.235806
upper limit	48.813584

Statistical analysis title	Treatment Comparison by Age Group
Statistical analysis description:	
Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 1.0 mg group	
Comparison groups	Zemuron 0.45 mg/kg – Neonates v Zemuron 1.0 mg/kg – Neonates
Number of subjects included in analysis	6
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1598
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-73.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-192.38825
upper limit	44.988253

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.6 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.6 mg/kg – Neonates v Zemuron 1.0 mg/kg – Neonates
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3355
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-53.988889
Confidence interval	
level	95 %
sides	2-sided
lower limit	-191.03828
upper limit	83.060501

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 0.6 mg group

Comparison groups	Zemuron 0.45 mg/kg – Infants v Zemuron 0.6 mg/kg – Infants
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0927
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-23.45303
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.954875
upper limit	5.048814

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.45 mg/kg – Infants v Zemuron 1.0 mg/kg – Infants
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0127
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-55.906566
Confidence interval	
level	95 %
sides	2-sided
lower limit	-95.650489
upper limit	-16.162642

Statistical analysis title Treatment Comparison by Age Group

Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.6 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.6 mg/kg – Infants v Zemuron 1.0 mg/kg – Infants
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1176
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-32.453535
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75.469399
upper limit	10.562328

Statistical analysis title Treatment Comparison by Age Group

Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 0.6 mg group

Comparison groups	Zemuron 0.45 mg/kg – Toddlers v Zemuron 0.6 mg/kg – Toddlers
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3246
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-5.936309

Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.076657
upper limit	6.20404

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.45 mg/kg – Toddlers v Zemuron 1.0 mg/kg – Toddlers
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-42.382389
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.931093
upper limit	-29.833684

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.6 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.6 mg/kg – Toddlers v Zemuron 1.0 mg/kg – Toddlers
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-36.44608
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.165781
upper limit	-23.726379

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 0.6 mg group

Comparison groups	Zemuron 0.45 mg/kg – Children v Zemuron 0.6 mg/kg – Children
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0107
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-14.769785
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.850735
upper limit	-3.688836

Statistical analysis title

Treatment Comparison by Age Group

Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.45 mg/kg – Children v Zemuron 1.0 mg/kg – Children
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-31.746668
Confidence interval	
level	95 %
sides	2-sided
lower limit	-43.580508
upper limit	-19.912829

Statistical analysis title

Treatment Comparison by Age Group

Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.6 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.6 mg/kg – Children v Zemuron 1.0 mg/kg – Children
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Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0019
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-16.976883
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.169156
upper limit	-6.78461

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 0.6 mg group

Comparison groups	Zemuron 0.45 mg/kg – Adolescents v Zemuron 0.6 mg/kg – Adolescents
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.098
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-10.077731
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.128534
upper limit	1.973072

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.45 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.45 mg/kg – Adolescents v Zemuron 1.0 mg/kg – Adolescents
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-26.591007

Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.145401
upper limit	-14.036614

Statistical analysis title	Treatment Comparison by Age Group
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Statistical analysis description:

Two-way ANOVA model including terms treatment group and site. Difference in least squares means is 0.6 mg/kg group minus 1.0 mg group

Comparison groups	Zemuron 0.6 mg/kg – Adolescents v Zemuron 1.0 mg/kg – Adolescents
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0104
Method	ANOVA
Parameter estimate	Difference in least squares means
Point estimate	-16.513276
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.848623
upper limit	-4.177929

Secondary: Time to Onset of Maximum Neuromuscular Block

End point title	Time to Onset of Maximum Neuromuscular Block
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End point description:

The onset time, defined as the duration from end of administration of the Zemuron intubating dose to onset of maximum neuromuscular block, was measured. Onset of maximum neuromuscular block was identified as occurrence of the first T1 value (the first twitch of a TOF stimulation) which showed no further decline over three consecutive TOF stimulations following administration of the Zemuron intubating dose. Analysis population is the Per Protocol group, which is all participants who were randomized after protocol Amendment 2 (major revision to study), received study drug, had at least one efficacy parameter measured and did not have any major protocol violations. Also to be included, participant must have an evaluable assessment for this measure.

End point type	Secondary
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End point timeframe:

From end of administration of Zemuron intubating dose to onset of maximum neuromuscular block

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	7	4	9
Units: minutes				
arithmetic mean (standard deviation)	1.22 (± 0.67)	1.1 (± 0.67)	0.82 (± 0.67)	0.69 (± 0.35)

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	5	16	15
Units: minutes				
arithmetic mean (standard deviation)	0.52 (± 0.21)	0.41 (± 0.19)	0.83 (± 0.47)	0.67 (± 0.3)

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	20	16
Units: minutes				
arithmetic mean (standard deviation)	0.57 (± 0.32)	0.89 (± 0.42)	0.87 (± 0.33)	0.67 (± 0.21)

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	16	13	
Units: minutes				
arithmetic mean (standard deviation)	1.1 (± 0.38)	1.08 (± 0.47)	0.72 (± 0.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Neuromuscular Block

End point title	Maximum Neuromuscular Block
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End point description:

Maximum neuromuscular block was defined as 100% minus the first T1 (expressed as percent of control) which showed no further decline over three consecutive TOF stimulations following administration of the Zemuron intubating dose. Analysis population is the Per Protocol group, which is all participants who were randomized after protocol Amendment 2 (major revision to study), received study drug, had at least one efficacy parameter measured and did not have any major protocol violations. Also to be included, participant must have an evaluable assessment for this measure.

End point type	Secondary
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End point timeframe:

At onset of maximum neuromuscular block, estimated to be up to approximately 2 minutes following administration of the Zemuron intubating dose

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	7	4	9
Units: percent neuromuscular block				
arithmetic mean (standard deviation)	98.75 (± 2.5)	97.86 (± 2.73)	100 (± 0)	100 (± 0)

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	5	16	15
Units: percent neuromuscular block				
arithmetic mean (standard deviation)	99.5 (± 1.22)	100 (± 0)	100 (± 0)	100 (± 0)

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	20	16
Units: percent neuromuscular block				
arithmetic mean (standard deviation)	100 (± 0)	100 (± 0)	100 (± 0)	100 (± 0)

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	16	13	
Units: percent neuromuscular block				
arithmetic mean (standard deviation)	100 (± 0)	99.69 (± 1.25)	100 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time from End of Zemuron Intubating Dose to Reappearance of T1

End point title	Time from End of Zemuron Intubating Dose to Reappearance of T1
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End point description:

The duration from end of administration of the Zemuron intubating dose to reappearance of T1 was measured. Analysis population is the Per Protocol group, which is all participants who were randomized after protocol Amendment 2 (major revision to study), received study drug, had at least one efficacy parameter measured and did not have any major protocol violations. Also to be included, participant must have an evaluable assessment for this measure.

End point type	Secondary
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End point timeframe:

From end of administration of Zemuron intubating dose to reappearance of T1

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	6	4	9
Units: minutes				
arithmetic mean (standard deviation)	36.9 (± 12.25)	40.8 (± 23.7)	94.95 (± 22.85)	37.55 (± 19.97)

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	3	16	14
Units: minutes				
arithmetic mean (standard deviation)	49.01 (± 14.01)	94.08 (± 16.54)	29.75 (± 10.05)	35.18 (± 9.94)

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	20	16
Units: minutes				
arithmetic mean (standard deviation)	66.59 (± 22.48)	19.53 (± 4.51)	31.53 (± 9.33)	48 (± 14.7)

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	13	
Units: minutes				

arithmetic mean (standard deviation)	28.32 (± 11.69)	33.09 (± 12.93)	57.43 (± 23.19)	
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Statistical analyses

No statistical analyses for this end point

Secondary: Time from End of Zemuron Intubating Dose to Recovery of T4/T1 (TOF Fourth Twitch to First Twitch) Ratio to 0.7 (70%)

End point title	Time from End of Zemuron Intubating Dose to Recovery of T4/T1 (TOF Fourth Twitch to First Twitch) Ratio to 0.7 (70%)
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End point description:

The duration from end of administration of the Zemuron intubating dose to recovery of T4/T1 to 0.7 (70%) was measured. At complete recovery, the T4/T1 ratio is 1.0 (100%). Analysis population is the Per Protocol group, which is all participants who were randomized after protocol Amendment 2 (major revision to study), received study drug, had at least one efficacy parameter measured and did not have any major protocol violations. Also to be included, participant must have an evaluable assessment for this measure.

End point type	Secondary
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End point timeframe:

From end of administration of Zemuron intubating dose to T4/T1 ratio of 0.7 (70%)

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	3	1 ^[1]	5
Units: minutes				
arithmetic mean (standard deviation)	102.75 (± 30.88)	76.99 (± 28.56)	175.53 (± 0)	87.28 (± 20.08)

Notes:

[1] - For this arm, standard deviation (SD) of 0.0 indicates SD could not be calculated since N=1

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	2	12	11
Units: minutes				
arithmetic mean (standard deviation)	96.62 (± 22.08)	166.33 (± 57.66)	56.41 (± 23.17)	59.29 (± 16.39)

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	12	18	12
Units: minutes				
arithmetic mean (standard deviation)	113.33 (\pm 18.04)	37.25 (\pm 10.81)	57.98 (\pm 23.22)	66.99 (\pm 17.27)

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	15	8	
Units: minutes				
arithmetic mean (standard deviation)	56.72 (\pm 21.05)	66.61 (\pm 20.36)	77.9 (\pm 27)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time from End of Zemuron Intubating Dose to Recovery of T4/T1 Ratio to 0.8 (80%)

End point title	Time from End of Zemuron Intubating Dose to Recovery of T4/T1 Ratio to 0.8 (80%)
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End point description:

The duration from end of administration of the Zemuron intubating dose to recovery of T4/T1 to 0.8 (80%) was measured. At complete recovery, the T4/T1 ratio is 1.0 (100%). Analysis population is the Per Protocol group, which is all participants who were randomized after protocol Amendment 2 (major revision to study), received study drug, had at least one efficacy parameter measured and did not have any major protocol violations. Also to be included, participant must have an evaluable assessment for this measure.

End point type	Secondary
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End point timeframe:

From end of administration of Zemuron intubating dose to T4/T1 ratio of 0.8 (80%)

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	1 ^[2]	3
Units: minutes				
arithmetic mean (standard deviation)	117.5 (\pm 42.54)	79.54 (\pm 11.16)	179.53 (\pm 0)	100.42 (\pm 15.37)

Notes:

[2] - For this arm, SD of 0.0 indicates SD could not be calculated since N=1

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5	2	11	11
Units: minutes				
arithmetic mean (standard deviation)	103.21 (\pm 25.01)	187.2 (\pm 50.42)	58.14 (\pm 22.97)	66.04 (\pm 19.76)

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	9	12	17	12
Units: minutes				
arithmetic mean (standard deviation)	125.52 (\pm 19.13)	40.5 (\pm 11.87)	64.69 (\pm 24.19)	71.62 (\pm 19.41)

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	13	9	
Units: minutes				
arithmetic mean (standard deviation)	62.72 (\pm 27.69)	71.2 (\pm 23.82)	88.67 (\pm 30.09)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time from End of Zemuron Intubating Dose to Recovery of T4/T1 Ratio to 0.9 (90%)

End point title	Time from End of Zemuron Intubating Dose to Recovery of T4/T1 Ratio to 0.9 (90%)
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End point description:

The duration from end of administration of the Zemuron intubating dose to recovery of T4/T1 to 0.9 (90%) was measured. At complete recovery, the T4/T1 ratio is 1.0 (100%). Analysis population is the Per Protocol group, which is all participants who were randomized after protocol Amendment 2 (major revision to study), received study drug, had at least one efficacy parameter measured and did not have any major protocol violations. Also to be included, participant must have an evaluable assessment for this measure.

End point type	Secondary
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End point timeframe:

From end of administration of Zemuron intubating dose to T4/T1 ratio of 0.9 (90%)

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	2	1 ^[3]	3
Units: minutes				
arithmetic mean (standard deviation)	133.99 (± 59.5)	119.61 (± 42.72)	180.78 (± 0)	108.58 (± 4.69)

Notes:

[3] - For this arm, SD of 0.0 indicates SD could not be calculated since N=1

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	1 ^[4]	9	10
Units: minutes				
arithmetic mean (standard deviation)	111.18 (± 30.56)	255.58 (± 0)	65.13 (± 31.28)	68.13 (± 19.9)

Notes:

[4] - For this arm, SD of 0.0 indicates SD could not be calculated since N=1

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	12	13	9
Units: minutes				
arithmetic mean (standard deviation)	148.76 (± 22.15)	46.53 (± 15.2)	71.04 (± 28.95)	76.03 (± 26.81)

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	10	11	7	
Units: minutes				
arithmetic mean (standard deviation)	63.5 (± 31.97)	73.42 (± 24.75)	97.74 (± 34.42)	

Statistical analyses

No statistical analyses for this end point

Secondary: Intubation Score for Participants who had Successful First Attempt Intubations within 75 Seconds after Administration of Zemuron

End point title	Intubation Score for Participants who had Successful First Attempt Intubations within 75 Seconds after Administration of Zemuron
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End point description:

Intubation conditions were scored using 3-point scales as described by Viby-Mogensen et al (Acta Anaesthesiol Scand 1996;40:59-74): laryngoscopy (single item rated easy, fair or difficult), vocal cords ("position" rated abducted, intermediate or closed; "movement" rated none, moving or closing) and reaction to intubation ("movement of the limbs" rated none, slight or vigorous; "airway reactivity" rated none, diaphragm or sustained >10 seconds). The first, second and third rating levels were equated to scores of excellent, good and poor, respectively. Overall intubation condition was rated "excellent" if all 5 items were rated excellent, "good" if all were rated good or excellent, and "poor" if any was rated poor. Overall excellent/good rating was considered "clinically acceptable"; overall poor rating was "unacceptable." Analysis population is Per Protocol group. Also to be included, participant must have had successful first attempt intubation within 75 seconds after Zemuron dose.

End point type	Secondary
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End point timeframe:

Up to 75 seconds after administration of Zemuron

End point values	Zemuron 0.45 mg/kg – Neonates	Zemuron 0.6 mg/kg – Neonates	Zemuron 1.0 mg/kg – Neonates	Zemuron 0.45 mg/kg – Infants
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	4	3	9
Units: participants				
Acceptable – Excellent	1	3	2	6
Acceptable – Good	2	1	1	3
Unacceptable – Poor	0	0	0	0

End point values	Zemuron 0.6 mg/kg – Infants	Zemuron 1.0 mg/kg – Infants	Zemuron 0.45 mg/kg – Toddlers	Zemuron 0.6 mg/kg – Toddlers
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	4	11	11
Units: participants				
Acceptable – Excellent	2	3	5	9
Acceptable – Good	1	0	5	1
Unacceptable – Poor	1	1	1	1

End point values	Zemuron 1.0 mg/kg – Toddlers	Zemuron 0.45 mg/kg – Children	Zemuron 0.6 mg/kg – Children	Zemuron 1.0 mg/kg – Children
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	11	18	13
Units: participants				
Acceptable – Excellent	9	9	15	9
Acceptable – Good	4	2	3	3
Unacceptable – Poor	0	0	0	1

End point values	Zemuron 0.45 mg/kg – Adolescents	Zemuron 0.6 mg/kg – Adolescents	Zemuron 1.0 mg/kg – Adolescents	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	14	13	10	
Units: participants				
Acceptable – Excellent	9	9	8	
Acceptable – Good	5	4	2	
Unacceptable – Poor	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For non-serious adverse events (AEs), through in-trial period, which ends at stable neuromuscular recovery or administration of another muscle relaxant or a reversal agent, whichever occurs first. For serious AEs, up to 7 days post-surgery

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Zemuron 0.45 mg/kg
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Reporting group description:

Participants in all age groups combined who received a single IV bolus intubation dose of 0.45 mg/kg Zemuron

Reporting group title	Zemuron 1.0 mg/kg
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Reporting group description:

Participants in all age groups combined who received a single IV bolus intubation dose of 1.0 mg/kg Zemuron

Reporting group title	Zemuron 0.6 mg/kg
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Reporting group description:

Participants in all age groups combined who received a single IV bolus intubation dose of 0.6 mg/kg Zemuron

Serious adverse events	Zemuron 0.45 mg/kg	Zemuron 1.0 mg/kg	Zemuron 0.6 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 66 (6.06%)	0 / 57 (0.00%)	3 / 66 (4.55%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	0 / 57 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Ventricular septal defect			
subjects affected / exposed	1 / 66 (1.52%)	0 / 57 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Lymphocele			
subjects affected / exposed	0 / 66 (0.00%)	0 / 57 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrioventricular block, complete			
subjects affected / exposed	1 / 66 (1.52%)	0 / 57 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 66 (1.52%)	0 / 57 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrospinal fistula			
subjects affected / exposed	0 / 66 (0.00%)	0 / 57 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 66 (0.00%)	0 / 57 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	0 / 66 (0.00%)	0 / 57 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia sepsis			
subjects affected / exposed	0 / 66 (0.00%)	0 / 57 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incision site abscess			

subjects affected / exposed	0 / 66 (0.00%)	0 / 57 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 57 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Zemuron 0.45 mg/kg	Zemuron 1.0 mg/kg	Zemuron 0.6 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 66 (18.18%)	16 / 57 (28.07%)	14 / 66 (21.21%)
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	9 / 66 (13.64%)	10 / 57 (17.54%)	11 / 66 (16.67%)
occurrences (all)	9	10	11
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	4 / 66 (6.06%)	7 / 57 (12.28%)	5 / 66 (7.58%)
occurrences (all)	4	7	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2004	Amendment 01: Primary reason for amendment was to update list of investigators/trial centers.
15 September 2005	Amendment 02: Primary reason for amendment was to exclude use of IV lidocaine and glycopyrrolate, define use of fentanyl for induction/maintenance of anesthesia, redefine the age groups for study participants, permit direct measurements of ventilatory parameters, include measurement of central body temperature, revise directions for induction with sevoflurane and description of boundary conditions for arterial oxygen percent saturation (SAO2) and end-tidal carbon dioxide (ETCO2), clarify description of reduction of sevoflurane after intubation, revise the blood sampling schedules and include reporting of Medical Device Reporting (MDR) reportable events.
07 December 2005	Amendment 03: Primary reason for amendment was to define use of local anesthetics for premedication and during surgery, define duration of induction of anesthesia, revise directions for administration of Zemuron for intubation, revise directions for measuring ventilatory parameters, revise the description of boundary conditions for SAO2 and include a requirement for obtaining acceptable practice neuromuscular recordings before neuromuscular transmission evaluation.
20 January 2006	Amendment 04: Primary reason for amendment was to indicate that non-United States (non-US) sites would not be conducting the trial under the US Investigational New Drug (IND) authorization, include assessment of appropriateness to initiate laryngoscopy at 60 seconds after administration of Zemuron, specify criteria for vital signs and electrocardiogram (ECG) findings that are considered to be adverse events, specify that any signs of histamine release should be captured as adverse events, clarify procedures for blinding assessor of intubation conditions and revise criteria for clinically significant abnormal values for cardiovascular parameters.
28 September 2006	Amendment 05: Primary reason for amendment was to add the use of epidural/caudal anesthesia to general anesthesia.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
15 June 2005	The P05798 protocol was performed under a US Food and Drug Administration (FDA) Pediatric Written Request (PWR). The protocol was amended several times in response to PWR amendments, FDA's comments on the protocol, changing FDA directives regarding the collection of data in clinical trials (e.g., FDA directive for collecting ethnicity data) or in response to requests from the trial site Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs). The major revisions to the protocol introduced in Protocol Amendments 2, 3 and 4 substantially altered trial conditions and assessment parameters. The trial was temporarily suspended during this period, and re-initiated after Protocol Amendment 4.	15 March 2006

Notes:

Limitations and caveats

None reported