

**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 | v2 (current) |
| This version publication date | 28 March 2019 |
| First version publication date | 17 March 2016 |
| Version creation reason | |

Trial information**Trial identification**

| | |
|-----------------------|--------|
| Sponsor protocol code | P05798 |
|-----------------------|--------|

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) | 55 |
| Adolescents (12-17 years) | 57 |
| 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 |
|------------------|------------------------------|

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 |
|------------------|------------------------------|

Arm description:

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

| 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 |
| 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 |
| 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 |
| 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 | |

| 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 |
| 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 |
| 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) |
|-----------------|--|

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 |
|----------------|---------|

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) | 35.30 (± 11.26) | 41.77 (± 11.60) |

| 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 (± 19.40) | |

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 0.6 mg/kg – Neonates v Zemuron 0.45 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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------------------------|-----------------------------------|

| | |
|--|--|
| 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 |

| | |
|---|-----------------------------------|
| 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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------------------------|-----------------------------------|

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 |
|-----------------|--|

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 |
|----------------|-----------|

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) | 1.10 (± 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 (± 0.30) |

| 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) | 1.10 (± 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 |
|-----------------|-----------------------------|

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 |
| 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 (± 2.50) | 97.86 (± 2.73) | 100.00 (± 0.00) | 100.00 (± 0.00) |

| 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) | 99.50 (± 1.22) | 100.00 (± 0.00) | 100.00 (± 0.00) | 100.00 (± 0.00) |

| 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) | 100.00 (± 0.00) | 100.00 (± 0.00) | 100.00 (± 0.00) | 100.00 (± 0.00) |

| 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) | 100.00 (± 0.00) | 99.69 (± 1.25) | 100.00 (± 0.00) | |

Statistical analyses

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 |
|-----------------|--|

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 |
|----------------|-----------|

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) | 36.90 (± 12.25) | 40.80 (± 23.70) | 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) | 48.00 (± 14.70) |

| 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 (\pm 11.69) | 33.09 (\pm 12.93) | 57.43 (\pm 23.19) | |

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%) |
|-----------------|--|

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 |
|----------------|-----------|

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 (\pm 30.88) | 76.99 (\pm 28.56) | 175.53 (\pm 0.0) | 87.28 (\pm 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 (\pm 22.08) | 166.33 (\pm 57.66) | 56.41 (\pm 23.17) | 59.29 (\pm 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%) |
|-----------------|--|

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 |
|----------------|-----------|

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 0.0) | 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 |
|-------------------------|-----------------------------|-----------------------------|-------------------------------|------------------------------|

| | | | | |
|--------------------------------------|-----------------------|----------------------|----------------------|----------------------|
| 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%) |
|-----------------|--|

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 |
|----------------|-----------|

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 (± 0.0) | 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 (± 0.0) | 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 |
|-----------------|--|

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 |
|----------------|-----------|

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 |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 10.0 |

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Zemuron 0.45 mg/kg |
|-----------------------|--------------------|

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 0.6 mg/kg |
|-----------------------|-------------------|

Reporting group description:

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

| | |
|-----------------------|-------------------|
| Reporting group title | Zemuron 1.0 mg/kg |
|-----------------------|-------------------|

Reporting group description:

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

| Serious adverse events | Zemuron 0.45 mg/kg | Zemuron 0.6 mg/kg | Zemuron 1.0 mg/kg |
|---|--------------------|-------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | 3 / 66 (4.55%) | 0 / 57 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | 0 / 66 (0.00%) | 0 / 57 (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 / 66 (0.00%) | 0 / 57 (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%) | 1 / 66 (1.52%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrioventricular block, complete | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | 0 / 66 (0.00%) | 0 / 57 (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 / 66 (0.00%) | 0 / 57 (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%) | 1 / 66 (1.52%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 66 (0.00%) | 1 / 66 (1.52%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnea | | | |
| subjects affected / exposed | 0 / 66 (0.00%) | 1 / 66 (1.52%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 66 (0.00%) | 1 / 66 (1.52%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision site abscess | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 66 (0.00%) | 1 / 66 (1.52%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 66 (1.52%) | 0 / 66 (0.00%) | 0 / 57 (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 0.6 mg/kg | Zemuron 1.0 mg/kg |
|---|--------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 66 (18.18%) | 14 / 66 (21.21%) | 16 / 57 (28.07%) |
| Injury, poisoning and procedural complications | | | |
| Procedural pain | | | |
| subjects affected / exposed | 9 / 66 (13.64%) | 11 / 66 (16.67%) | 10 / 57 (17.54%) |
| occurrences (all) | 9 | 11 | 10 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 66 (6.06%) | 5 / 66 (7.58%) | 7 / 57 (12.28%) |
| occurrences (all) | 4 | 5 | 7 |

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