ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 03/17/2011

ClinicalTrials.gov ID: NCT00436345

Study Identification

Unique Protocol ID:	108701
Brief Title:	Pharmacoeconomic Consequences Of Analgesia in the Intensive Care Unit (ICU)
Official Title:	A Randomized, Open Label, Multicentre Study to Compare the Pharmaco-economic Implications of an Analgesia Based Regimen With Remifentanil and a Conventional Sedation Based Regimen Using Propofol in Medical and Post-surgical ICU Subjects Requiring Mechanical Ventilation for at Least 2 Days.
Secondary IDs:	

Study Status

Record Verification:	March 2011
Overall Status:	Terminated
Study Start:	November 2007
Primary Completion:	August 2008 [Actual]
Study Completion:	September 2008 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	
Collaborators:	

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: N. 206994 Board Name: Comitato Etico Azienda Ospedaliero universitaria Ospedali Riuniti Umberto I°- G.M. Lancisi - G.Salesi Board Affiliation: not affiliated Phone: 0039-071596 Email: m.ciarroc@ao-umbertoprimo.marche.it
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Italy: Ethics Committee

Study Description

Brief Summary:	This study will be a multicentre randomized, open-label, phase IIIb study. This study will evaluate two different techniques of sedation: an analgesia based regimen with remifentanil versus a conventional sedation based regimen using propofol in subjects that require mechanical ventilation for at least 2 days in the ICU. The conventional sedation based regimen will consist of propofol combined with an opioid according to routine clinical practice (morphine, fentanyl, sufentanil or other as required) . The analgesia based regimen will consist of remifentanil, with propofol added on if required.
Detailed Description:	

Conditions

Conditions:	Analgesia
Keywords:	analgesia Mechanical ventilation pharmaco-economic ICU

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label

Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	39 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Remifentanil remifentanil	Drug: Remifentanil analgesia in medical and post-surgical Intensive Care Unit subjects requiring mechanical ventilation
Active Comparator: Propofol Propofol infusion	Drug: Propofol conventional sedation in medical and post-surgical Intensive Care Unit subjects requiring mechanical

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Medical and post-surgical patients admitted to ICU and requiring mechanical ventilation.
- Intubated subjects expected to require mechanical ventilation for longer than 48 hours after starting the study drug.
- Subjects requiring both analgesia and sedation with a regimen comprising a hypnotic agent and an opioid.

Exclusion Criteria:

- Diagnosis: cardiopulmonary resuscitation (CPR) in the previous 24 hours or expecting to require major surgery within the next three days
- Subject who, in the judgement of the investigator, has a life expectancy of 2 days or refrained or refuses full life support, which would limit the care provided
- Concurrent medications:
  - Requires or is likely to require neuromuscular blocking agents by continuous infusion to facilitate mechanical ventilation
  - Has or is likely to receive an epidural block during the treatment period

Contacts/Locations

Study Officials: GSK Clinical Trials
Study Director
GlaxoSmithKline

Locations: Italy
GSK Investigational Site
Udine, Friuli-Venezia-Giulia, Italy, 33100

GSK Investigational Site
Roma, Lazio, Italy, 00161

GSK Investigational Site
Palermo, Sicilia, Italy, 90127

GSK Investigational Site
Ferrara, Emilia-Romagna, Italy, 44100

GSK Investigational Site
Catanzaro, Calabria, Italy, 88100

GSK Investigational Site
Napoli, Campania, Italy, 80131

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Overall Study

	Remifentanil	Propofol
Started	21	18
Completed	18	18
Not Completed	3	0
ICU resident beyond follow-up period	3	0

Baseline Characteristics

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Baseline Measures

	Remifentanil	Propofol	Total
Number of Participants	21	18	39

	Remifentanil	Propofol	Total
Age, Continuous [units: years] Mean (Standard Deviation)	62.1 (10.7)	60.2 (14.3)	61.23 (12.32)
Gender, Male/Female [units: participants]			
Female	11	7	18
Male	10	11	21
Race/Ethnicity, Customized [units: participants]			
White	21	17	38
Asian	0	1	1
Simplified acute physiology score (SAPS II) score [1] [units: Points on a scale] Mean (Standard Deviation)	25.7 (16.7)	20.9 (16.1)	23.23 (16.30)

[1] The SAPS II score consists of adding the points from 17 variables: age, 12 physiological variables, type of admission, and 3 chronic disease variables. These variables are added to give a SAPS II score with a range of 0 ("predicted mortality" 0%) to 163 ("predicted mortality" 100%). SAPS II data were collected from local laboratories for 24 hours following ICU admission.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Duration of Time on Mechanical Ventilation (Intent-to-Treat Population)
Measure Description	Time from start of mechanical ventilation until actual extubation (the process of removing a tube from the airway).
Time Frame	Up to 38 days (912 hours)
Safety Issue?	No

Analysis Population Description

Intent-to-Treat (ITT) Population: all randomised participants who had taken at least one dose of study medication

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	21	18
Duration of Time on Mechanical Ventilation (Intent-to-Treat Population) [units: Hours (hr)] Mean (Standard Error)	77 (8.31)	70 (6.48)

2. Primary Outcome Measure:

Measure Title	Duration of Time on Mechanical Ventilation (Modified-Intent-to-Treat Population)
Measure Description	Time from start of mechanical ventilation until actual extubation.
Time Frame	Up to 38 days (912 hours)
Safety Issue?	No

Analysis Population Description

Modified-Intent-to-Treat (mITT) Population: all randomised participants who had taken at least one dose of study medication and who had efficacy measurements

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.

	Description
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	21	18
Duration of Time on Mechanical Ventilation (Modified-Intent-to-Treat Population) [units: Hours] Mean (Standard Error)	77 (8.31)	70 (6.48)

3. Primary Outcome Measure:

Measure Title	Duration of Time on Mechanical Ventilation (Per-Protocol Population)
Measure Description	Time from start of mechanical ventilation until actual extubation
Time Frame	Up to 38 days (912 hours)
Safety Issue?	No

Analysis Population Description

Per-Protocol (PP) Population: all participants from the MITT population without any major protocol violation

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	11	13

	Remifentanil	Propofol
Duration of Time on Mechanical Ventilation (Per-Protocol Population) [units: Hours] Mean (Standard Error)	87 (9.47)	81 (4.71)

4. Secondary Outcome Measure:

Measure Title	Duration of Time in Intensive Care Unit (ICU) and Potential Stay in ICU (the Time Expected for Extubation, i.e., the Time Between Intubation and Eligibility for Extubation, According to Investigator's Decision)
Measure Description	Duration of Intensive Care Unit (ICU) stay and the duration of potential stay in the ICU were measured.
Time Frame	Up to 38 days (912 hours)
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants with available ICU data were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	12	14
Duration of Time in Intensive Care Unit (ICU) and Potential Stay in ICU (the Time Expected for Extubation, i.e., the Time Between Intubation and Eligibility for Extubation, According to Investigator's Decision) [units: Hours] Mean (Standard Deviation)		

	Remifentanil	Propofol
Duration of ICU stay	212.6 (163.4)	208.5 (185.2)
Duration of potential ICU stay	211.3 (161.4)	208.1 (185.1)

5. Secondary Outcome Measure:

Measure Title	Duration of Extubation
Measure Description	Duration of extubation was measured.
Time Frame	up to 38 days (912 hours)
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants with available extubation data were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	13	12
Duration of Extubation [units: hours] Mean (Standard Deviation)	0.4 (0.5)	0.7 (0.8)

6. Secondary Outcome Measure:

Measure Title	Duration of Weaning

Measure Description	Duration of weaning (the time from the intubation until the recovery of natural respiratory ability) was measured.
Time Frame	up to 38 days (912 hours)
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants for which data are available were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	19	14
Duration of Weaning [units: hours] Mean (Standard Deviation)	0.42 (1.0)	0.26 (0.3)

7. Secondary Outcome Measure:

Measure Title	Duration of Remifentanil Infusion (ITT Population)
Measure Description	Data for this measure come from the infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	Up to 10 days (240 hours)
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants infused with Remifentanil were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	21	0
Duration of Remifentanil Infusion (ITT Population) [units: Hours] Mean (Standard Deviation)	67.7 (60.3)	

8. Secondary Outcome Measure:

Measure Title	Duration of Propofol Infusion (ITT Population)
Measure Description	Data for this measure come from the infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	up to 10 days (240 hours)
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants infused with Propofol were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.

	Description
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	13	18
Duration of Propofol Infusion (ITT Population) [units: hours] Mean (Standard Deviation)	47.6 (41.8)	86.2 (89.4)

9. Secondary Outcome Measure:

Measure Title	Duration of Sufentanil, Fentanil, and Morphine Infusion (ITT Population)
Measure Description	Data for this measure come from the infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	up to 10 days (240 hours)
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants infused with Sufentanil, Fentanil, and Morphine were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	0	8

	Remifentanil	Propofol
Duration of Sufentanil, Fentanil, and Morphine Infusion (ITT Population) [units: hours] Mean (Standard Deviation)		
Sufentanil, n=8		51.2 (15.42)
Fentanil, n=5		47.5 (40.7)
Morphine, n=1		0.03 (0.0)

10. Secondary Outcome Measure:

Measure Title	Dose of Remifentanil Administered - Continuous Infusion
Measure Description	Data for this measure come from infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	Up to 10 days
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants dosed with Remifentanil were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	21	0
Dose of Remifentanil Administered - Continuous Infusion [units: ug/kg/h (micrograms per kilogram per hr)]	10.6 (7.2)	

	Remifentanil	Propofol
Mean (Standard Deviation)		

11. Secondary Outcome Measure:

Measure Title	Doses of Sufentanil and Fentanil Administered - Continuous Infusion
Measure Description	Data for this measure come from infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	up to 10 days
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants dosed with Remifentanil were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	0	8
Doses of Sufentanil and Fentanil Administered - Continuous Infusion [units: ug/kg/h] Mean (Standard Deviation)		
Sufentanil, n=8		0.2 (0.1)
Fentanil, n=5		5.0 (7.5)

12. Secondary Outcome Measure:

Measure Title	Dose of Propofol Administered - Continuous Infusion
Measure Description	Data for this measure come from infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	Up to 10 days
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants dosed with Propofol were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	13	18
Dose of Propofol Administered - Continuous Infusion [units: mg/kg/h (milligrams per kilogram per hr)] Mean (Standard Deviation)	2.3 (4.0)	1.8 (1.3)

13. Secondary Outcome Measure:

Measure Title	Dose of Morphine Administered - Continuous Infusion
Measure Description	Data for this measure come from infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	up to 10 days
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants dosed with Morphine were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	0	1
Dose of Morphine Administered - Continuous Infusion [units: mg/kg/h] Mean (Standard Deviation)		4.3 (0.0)

14. Secondary Outcome Measure:

Measure Title	Total Dose of Propofol Administered - Bolus
Measure Description	Data from this measure come from infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	Up to 10 days
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants dosed with Propofol were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.

	Description
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	4	4
Total Dose of Propofol Administered - Bolus [units: mg/kg] Mean (Standard Deviation)	1.5 (0.4)	5.5 (4.5)

15. Secondary Outcome Measure:

Measure Title	Total Dose of Fentanil Administered - Bolus
Measure Description	Data for this measure come from infusion pump display; the infusion pump infuses medication (analgesics and sedative agents) into the participant's circulatory system.
Time Frame	Up to 10 days
Safety Issue?	No

Analysis Population Description

ITT Population. Only participants dosed with Fentanil were analyzed.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	0	5

	Remifentanil	Propofol
Total Dose of Fentanil Administered - Bolus [units: ug/kg] Mean (Standard Deviation)		5.1 (3.6)

16. Secondary Outcome Measure:

Measure Title	Number of Participants Analyzed for Sedation - Agitation Scale (SAS) and Pain Intensity (PI) Scale
Measure Description	Data from participants in the study for which the Sedation–Agitation Scale (SAS) and Pain Intensity (PI) were recorded were analyzed. “Sedation - Agitation” was assessed, using the “Riker Sedation-Agitation Scale” (SAS), by the following 7-point scale: 7, dangerous agitation; 6, very agitated; 5, agitated; 4, calm, cooperative; 3, sedated; 2, very sedated; 1, unarousable. “Pain Intensity” was assessed by the following 6-point Pain Intensity Scale: 1, no pain; 2, mild pain; 3, moderate pain; 4, severe pain; 5 very severe pain; 6, worst possible pain.
Time Frame	Up to 38 Days
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	21	18
Number of Participants Analyzed for Sedation - Agitation Scale (SAS) and Pain Intensity (PI) Scale [units: participants]		
Screening period	21	18

	Remifentanil	Propofol
Day 1	21	18
Day 2	18	17
Day 3	15	14
Day 4	10	11
Day 5	6	3
Day 6	2	2
Day 7	2	1
Day 8	1	0
Day 9	1	0
Day 10	1	0
Extubation period	12	12
Post-extubation period	5	6

17. Secondary Outcome Measure:

Measure Title	Sedation-Agitation From Screening Through the End of Study
Measure Description	"Sedation - Agitation" was assessed, using the "Riker Sedation-Agitation Scale" (SAS), by the following 7-point scale: 7, dangerous agitation; 6, very agitated; 5, agitated; 4, calm, cooperative; 3, sedated; 2, very sedated; 1, unarousable.
Time Frame	Up to 38 days
Safety Issue?	No

Analysis Population Description

mITT Population, according to the participants' status

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.

	Description
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	21	18
Sedation-Agitation From Screening Through the End of Study [units: Points on a scale] Mean (Standard Deviation)		
Screening period	3.5 (1.0)	3.7 (1.2)
Day 1	3.0 (0.9)	2.9 (0.8)
Day 2	2.8 (1.0)	2.9 (0.9)
Day 3	3.1 (0.8)	3.1 (0.6)
Day 4	3.4 (0.9)	3.1 (0.6)
Day 5	3.5 (0.4)	3.1 (1.1)
Day 6	3.9 (0.2)	2.6 (0.6)
Extubation period	3.2 (0.7)	3.6 (0.4)
Post-extubation period	3.8 (0.8)	4.0 (0.0)

18. Secondary Outcome Measure:

Measure Title	Sedation-Agitation for Day 7
Measure Description	“Sedation - Agitation” was assessed, using the “Riker Sedation-Agitation Scale” (SAS), by the following 7-point scale: 7, dangerous agitation; 6, very agitated; 5, agitated; 4, calm, cooperative; 3, sedated; 2, very sedated; 1, unarousable.
Time Frame	Day 7
Safety Issue?	No

Analysis Population Description

mITT Population according to the participants’ status

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	1	1
Sedation-Agitation for Day 7 [units: points on a scale] Mean (Standard Deviation)	4.0 (0.0)	3.3 (0.0)

19. Secondary Outcome Measure:

Measure Title	Sedation-Agitation From Day 8 to Day 10
Measure Description	“Sedation - Agitation” was assessed, using the “Riker Sedation-Agitation Scale” (SAS), by the following 7-point scale: 7, dangerous agitation; 6, very agitated; 5, agitated; 4, calm, cooperative; 3, sedated; 2, very sedated; 1, unarousable.
Time Frame	Days 8, 9, and 10
Safety Issue?	No

Analysis Population Description

mITT Population according to the participants’ status

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.

	Description
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	1	0
Sedation-Agitation From Day 8 to Day 10 [units: points on a scale] Mean (Standard Deviation)		
Day 8	4.0 (0.0)	
Day 9	3.3 (0.0)	
Day 10	3.6 (0.0)	

20. Secondary Outcome Measure:

Measure Title	Number of Participants Analyzed for BIS (Bispectral Index Scale)
Measure Description	Participants in the study for which BIS were evaluated. The BIS monitor provides a single dimensionless number, the BIS value, which ranges from 0 to 100. A BIS value of 0 equals electroencephalogram silence, near 100 is the expected value in a fully awake adult, and between 40 and 60 indicates a level for general anaesthesia.
Time Frame	Up to 38 days
Safety Issue?	No

Analysis Population Description

mITT Population

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.

	Description
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	5	0
Number of Participants Analyzed for BIS (Bispectral Index Scale) [units: participants]		
Screening period	3	
Day 1	4	
Day 2	4	
Day 3	5	
Day 4	4	
Day 5	1	
Day 6	0	
Day 7	0	
Day 8	0	
Day 9	0	
Day 10	0	
Extubation period	2	
Post-extubation period	2	

21. Secondary Outcome Measure:

Measure Title	Bispectral Index (BIS)
Measure Description	The BIS monitor provides a single dimensionless number, the BIS value, which ranges from 0 to 100. A BIS value of 0 equals electroencephalogram silence, near 100 is the expected value in a fully awake adult, and between 40 and 60 indicates a level for general anaesthesia.

Time Frame	Screening through End of Study, up to 38 days
Safety Issue?	No

Analysis Population Description

mITT Population. Due to the nonmandatory nature of BIS measure in the clinical practice, some participants did not have all the measures for all days in which they were in the study.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per killograms per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.

Measured Values

	Remifentanil
Number of Participants Analyzed	5
Bispectral Index (BIS) [units: Points on a scale] Mean (Standard Deviation)	
Screening period (n = 3, 0)	38.0 (4.6)
Day 1 (n = 4, 0)	47.3 (18.3)
Day 2 (n = 4, 0)	45.6 (16.8)
Day 3 (n = 5, 0)	45.8 (17.5)
Day 4 (n = 4, 0)	49.7 (13.3)

22. Secondary Outcome Measure:

Measure Title	Bispectral Index (BIS) for Day 5
Measure Description	The BIS monitor provides a single dimensionless number, the BIS value, which ranges from 0 to 100. A BIS value of 0 equals electroencephalogram silence, near 100 is the expected value in a fully awake adult, and between 40 and 60 indicates a level for general anaesthesia.
Time Frame	Day 5
Safety Issue?	No

Analysis Population Description

mITT Population. At Day 5, only one participant remained in the study; the others were already extubated.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	1	0
Bispectral Index (BIS) for Day 5 [units: points on a scale] Mean (Standard Deviation)	52.7 (0.0)	

23. Secondary Outcome Measure:

Measure Title	Bispectral Index (BIS) for Extubation Period and Post-Extubation Period
Measure Description	The BIS monitor provides a single dimensionless number, the BIS value, which ranges from 0 to 100. A BIS value of 0 equals electroencephalogram silence, near 100 is the expected value in a fully awake adult, and between 40 and 60 indicates a level for general anaesthesia.
Time Frame	up to 38 days
Safety Issue?	No

Analysis Population Description

mITT Population. The BIS value was recorded only for 2 participants, in the extubation and post-extubation periods.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	2	0
Bispectral Index (BIS) for Extubation Period and Post-Extubation Period [units: points on a scale] Mean (Standard Deviation)		
Extubation period	70.0 (0.0)	
Post-Extubation period	71.8 (1.1)	

24. Secondary Outcome Measure:

Measure Title	Pain Intensity (PI)
Measure Description	“Pain Intensity” was assessed by the following 6-point Pain Intensity Scale: 1, no pain; 2, mild pain; 3, moderate pain; 4, severe pain; 5 very severe pain; 6, worst possible pain.
Time Frame	Up to 38 days
Safety Issue?	No

Analysis Population Description

ITT Population, according to the participants' status. Participants remained in the study until they could be extubated; thus, the number of participants analyzed may vary by day.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	21	18
Pain Intensity (PI) [units: Points on a scale] Mean (Standard Deviation)		
Screening period, n=21, 18	1.3 (0.8)	1.2 (0.5)
Day 1, n=21, 18	1.3 (0.5)	1.1 (0.2)
Day 2, n=18, 17	1.2 (0.4)	1.1 (0.2)
Day 3, n=15, 14	1.2 (0.4)	1.1 (0.3)
Day 4, n=10, 11	1.2 (0.4)	1.0 (0.1)
Day 5, n=6, 3	1.3 (0.7)	1.0 (0.0)
Day 6, n=2, 2	1.0 (0.0)	1.0 (0.0)
Day 7, n=2, 1	1.0 (0.0)	1.0 (0.0)
Extubation period, n=12, 12	1.4 (0.8)	1.4 (0.6)
Post-extubation period, n=5, 6	2.0 (1.0)	1.3 (0.5)

25. Secondary Outcome Measure:

Measure Title	Pain Intensity From Day 8 to Day 10
Measure Description	“Pain Intensity” was assessed by the following 6-point Pain Intensity Scale: 1, no pain; 2, mild pain; 3, moderate pain; 4, severe pain; 5 very severe pain; 6, worst possible pain.
Time Frame	Days 8, 9, and 10

Safety Issue?	No

Analysis Population Description

mITT Population. Participants remained in the study until they could be extubated; thus, the number of participants analyzed may vary by day.

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Measured Values

	Remifentanil	Propofol
Number of Participants Analyzed	1	0
Pain Intensity From Day 8 to Day 10 [units: points on a scale] Mean (Standard Deviation)		
Day 8	1.0 (0.0)	
Day 9	1.0 (0.0)	
Day 10	1.0 (0.0)	

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Remifentanil	Infusion started between 6 and 9 ug/kg/h (micrograms per kilogram per hour), and titrated in 1.5 ug/kg/h increments at 5-10 minute intervals to achieve a level of adequate sedation based on investigator clinical judgement. The maximum dose rate was 45 ug/kg/h. Once the remifentanil infusion rate reached 12 ug/kg/h, the sedative infusion (propofol) could be administered if level of sedation was not adequate.
Propofol	The administration of propofol combined with an opioid (fentanyl, sufentanil, morphine, or other) as required to maintain adequate analgesia/sedation and stable haemodynamics was performed according to routine clinical practice for the investigational site, and in accordance with standard clinical protocols.

Serious Adverse Events

	Remifentanil	Propofol
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/21 (0%)	0/18 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Remifentanil	Propofol
	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/	3/
Cardiac disorders		
Bradycardia [A] †	0/21 (0%)	1/18 (5.56%)
Gastrointestinal disorders		
Ascites [A] †	1/21 (4.76%)	0/18 (0%)
Respiratory, thoracic and mediastinal disorders		
Apnoea [A] †	2/21 (9.52%)	0/18 (0%)
Respiratory depression [A] †	1/21 (4.76%)	0/18 (0%)
Respiratory failure [A] †	1/21 (4.76%)	0/18 (0%)
Skin and subcutaneous tissue disorders		
Oedema at surgical site [A] †	0/21 (0%)	1/18 (5.56%)
Vascular disorders		

	Remifentanil	Propofol
	Affected/At Risk (%)	Affected/At Risk (%)
Hypertension [A] †	5/21 (23.81%)	1/18 (5.56%)
Hypotension [A] †	2/21 (9.52%)	0/18 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

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