Clinical trial results:
Therapeutic Equivalence Study of Propofol Using Target-Controlled Infusion of Propofol 2% (20 mg/mL) MCT Fresenius Compared with Diprivan 20 mg/mL (AstraZeneca) in Patients Undergoing Elective Surgery

Summary

EudraCT number	2012-005701-43
Trial protocol	FR
Global end of trial date	13 February 2014

Results information

Result version number	v1 (current)
This version publication date	08 April 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	PROP-001-CP3

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01856998
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fresenius Kabi Deutschland GmbH
Sponsor organisation address	Else-Kröner-Str. 1, Bad Homburg, Germany, 61352
Public contact	Division Medical & Clinical Affairs Generics & Standard Solutions, Volume Therapy, Fresenius Kabi Deutschland GmbH, scientific-contact@fresenius-kabi.com
Scientific contact	Division Medical & Clinical Affairs Generics & Standard Solutions, Volume Therapy, Fresenius Kabi Deutschland GmbH, scientific-contact@fresenius-kabi.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 March 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2014
Global end of trial reached?	Yes
Global end of trial date	13 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the therapeutic equivalence, based on pharmacodynamic parameters, of Propofol 2% (20 mg/mL) MCT Fresenius and Diprivan 20 mg/mL (AstraZeneca) administered by target-controlled infusion (TCI)

Protection of trial subjects:

It was the responsibility of the Investigator to obtain a signed informed consent form from all patients prior to inclusion in the study.
After administration of propofol, the patient was observed for an appropriate period of time. Circulatory and respiratory functions were constantly monitored (e.g. electrocardiogram [ECG], pulse oximetry) and facilities for maintenance of patient airways, artificial ventilation, and other resuscitation facilities were immediately available at all times.
For sedation during surgical and diagnostic procedures, propofol was not administered by the same person conducting the surgical or diagnostic procedure. Infusion of colloids was to replace estimated blood loss in a 1:1 ratio with continuous infusion of iso-oncotic colloid. The type of colloid product used was selected as per standard of care.
Suspected hypovolaemia could have been treated with boluses of colloid solution in increments of 100 to 250 mL. If hypovolaemia was not a threat to the welfare of the patient, colloid administration was to be kept to ≤500 mL.
Prior to emergence from anaesthesia the patient could have been administered medication for post operative nausea and vomiting as per local standard of care.
The patient was monitored and received post-anaesthesia care as per local standard of care.
Patients were determined eligible for discharge from the peri-procedural setting as per local standard of care, but were not allowed to go home unaccompanied.
If discharged home, the patient was instructed not to consume alcohol, to drive, to operate machinery, or to work in potentially hazardous situations for a suitable period following recovery from anaesthesia as per local standard of care.

Background therapy: -

Evidence for comparator:

Propofol was first developed and patented by ICI (now AstraZeneca), marketed under the proprietary name Diprivan

Actual start date of recruitment	28 May 2013
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	France: 71
Worldwide total number of subjects	71
EEA total number of subjects	71

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	70
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was monocentric and conducted in France. 1st patient was enrolled on 28 May 2013 and last patient completed the study on 13 Feb 2014. A total of 71 patients were enrolled of whom 70 were randomised: 35 to Propofol MCT Fresenius and 35 to Diprivan. All randomised patients received treatment as per the protocol and all completed the study.

Pre-assignment

Screening details:

Included were male and female patients, ≥18 to <65 years of age, with ASA physical status 1 or 2 and undergoing elective, minor orthopaedic, vascular, urological, and gynaecological surgery.
One patient was enrolled but not randomised to treatment; patient was deemed a screening failure due to violation of an exclusion criterion.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Blinding implementation details:

All study procedures in the surgery room were performed by a blinded anaesthetist and a blinded nurse. Randomisation and blinding procedures (preparation of syringes) were performed by another unblinded nurse, in another room. The empty used study drug vials were packed and carried back to the pharmacy for storage before the unblinded monitoring visit, performed by an unblinded monitor.

Arms

Are arms mutually exclusive?	Yes
Arm title	Propofol 2% (20 mg/mL) MCT Fresenius

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Propofol 2% (20 mg/mL) MCT Fresenius
Investigational medicinal product code	
Other name	Propofol 20 mg/ml
Pharmaceutical forms	Emulsion for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dosage: Initial effect-site target concentration: 5 µg/mL, if necessary increased by 1 µg/mL every 60 seconds until Loss of Eyelash Reflex (LOER).

Frequency: Continuously (was adjusted to keep Bispectral Index (BIS) between 40 and 60, however maintenance target concentration could have been increased if a patient needs a BIS <40 with regard to individual condition and the respective surgery).

Duration: Until end of surgery

Arm title	Diprivan 20 mg/mL (AstraZeneca)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Diprivan 20 mg/mL (AstraZeneca)
Investigational medicinal product code	
Other name	Propofol 20 mg/ml
Pharmaceutical forms	Emulsion for injection/infusion in pre-filled syringe
Routes of administration	Intravenous use

Dosage and administration details:

Dosage: Initial effect-site target concentration: 5 µg/mL; if necessary increased by 1 µg/mL every 60 seconds until Loss of Eyelash Reflex (LOER).

Frequency: Continuously (was adjusted to keep Bispectral Index (BIS) between 40 and 60, however maintenance target concentration could have been increased if a patient needed a BIS <40 with regard to individual condition and the respective surgery).

Duration: Until end of surgery

Number of subjects in period 1[1]	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)
Started	35	35
Completed	35	35

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: In this study 'enrolled patients' defines all patients who had provided informed consent for this study (N=71). One of the 71 enrolled patients was not randomised to treatment and thus has not entered the baseline period. Therefore only 70 patients entered the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Propofol 2% (20 mg/mL) MCT Fresenius
Reporting group description: -	
Reporting group title	Diprivan 20 mg/mL (AstraZeneca)
Reporting group description: -	

Reporting group values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)	Total
Number of subjects	35	35	70
Age categorical Units: Subjects			
Adults (18-64 years)	35	34	69
From 65-84 years	0	1	1
Age continuous Units: years			
arithmetic mean	44.6	48	
standard deviation	± 10.54	± 9.39	-
Gender categorical Units: Subjects			
Female	12	17	29
Male	23	18	41

End points

End points reporting groups

Reporting group title	Propofol 2% (20 mg/mL) MCT Fresenius
Reporting group description: -	
Reporting group title	Diprivan 20 mg/mL (AstraZeneca)
Reporting group description: -	

Primary: Time to Loss of Eyelash Reflex (LOER)

End point title	Time to Loss of Eyelash Reflex (LOER)

End point description:

The study drug infusion was administered beginning at an initial effect-site target propofol concentration of 5 µg/mL.

LOER was to be assessed by gently touching the patient's eyelashes. If LOER had not occurred within 150 seconds of starting study drug infusion, target propofol effect-site concentration was to be increased by 1 µg/mL every 60 seconds until LOER was observed.

End point type	Primary

End point timeframe:

LOER was to be assessed every 10 seconds from the initiation of TCI anaesthesia (device mediated study drug infusion) until LOER occurred up to 150 seconds.
The overall timeframe until LOER is observed varies from patient to patient.

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34[1]	35[2]		
Units: Minutes				
arithmetic mean (standard deviation)	2.602 (± 1.49412)	2.5096 (± 1.40146)		

Notes:

[1] - Intention-to-treat (ITT) analysis set

[2] - Intention-to-treat (ITT) analysis set

Statistical analyses

Statistical analysis title	Therapeutic Equivalence

Statistical analysis description:

No formal statistical inference was required by the ANSM (French Health Authority). But a descriptive comparison of the primary endpoint (time to LOER) between the test and reference treatment was performed using analysis of variance (ANOVA) with a single fixed effect for treatment. This analysis was specified as descriptive since the study was not powered for the comparison. Treatment difference (test – reference) with 90% confidence intervals (CI) are presented for the ITT population.

Comparison groups	Propofol 2% (20 mg/mL) MCT Fresenius v Diprivan 20 mg/mL (AstraZeneca)

Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (final values)
Point estimate	0.092
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.489
upper limit	0.674

Secondary: Time to Bispectral Index 50

End point title	Time to Bispectral Index 50

End point description:

Throughout the surgical procedure, the propofol target effect-site concentration was to be adjusted to maintain the Bispectral Index (BIS) at 40 to 60. A lower BIS was permissible if the Investigator providing anaesthesia considered it as clinically required for maintenance of adequate anaesthesia.

End point type	Secondary

End point timeframe:

A stopwatch was used to assess the time to BIS 50. The start of the stopwatch coincided directly with initiation of infusion of the study drug. The time to BIS 50 was taken at the first occasion BIS 50 was recorded on the BIS monitor.

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	35		
Units: Minutes				
arithmetic mean (standard deviation)	3.6089 (± 1.95474)	4.5033 (± 2.72717)		

Statistical analyses

No statistical analyses for this end point

Secondary: Predicted Effect-site Propofol Concentrations at Time of LOER

End point title	Predicted Effect-site Propofol Concentrations at Time of LOER

End point description:

Patient-level predicted effect-site propofol concentrations were extracted from the infusion pump data.

End point type	Secondary

End point timeframe:

Measured after initiation of infusion of the study drug at the timepoint where the LOER occured.

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	34		
Units: µg/ml				
arithmetic mean (standard deviation)	5.088 (± 0.4568)	5.143 (± 0.6714)		

Statistical analyses

No statistical analyses for this end point

Secondary: Predicted Effect-site Propofol Concentrations at Time of BIS 50

End point title	Predicted Effect-site Propofol Concentrations at Time of BIS 50

End point description:

Patient-level predicted effect-site propofol concentrations were extracted from the infusion pump data.

End point type	Secondary

End point timeframe:

Measured at the timepoint where the BIS 50 value was recorded on the BIS monitor for the 1st occasion after initiation of infusion of the study drug.

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	33		
Units: µg/ml				
arithmetic mean (standard deviation)	5.122 (± 0.4547)	5.454 (± 0.857)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Propofol Concentration 2 (+/- 1) minutes after infusion start

End point title	Plasma Propofol Concentration 2 (+/- 1) minutes after infusion start

End point description:

Secondary Pharmacokinetic (PK) outcome variables

End point type	Secondary

End point timeframe:

2 (+/- 1) minutes after infusion start

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30[3]	26[4]		
Units: µg/ml				
median (inter-quartile range (Q1-Q3))	3.4 (2.3 to 4.7)	3.4 (2.6 to 4.3)		

Notes:

[3] - PK analysis set

[4] - PK analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Propofol Concentration 10 (+/- 2) minutes after infusion start

End point title	Plasma Propofol Concentration 10 (+/- 2) minutes after infusion start

End point description:

Secondary PK outcome variables

End point type	Secondary

End point timeframe:

10 (+/- 2) minutes after infusion start

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	17		
Units: µg/ml				
median (inter-quartile range (Q1-Q3))	4.05 (2.75 to 5)	5.5 (4.2 to 6.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Propofol Concentration 10 minutes after achieving target concentration

End point title	Plasma Propofol Concentration 10 minutes after achieving target concentration

End point description:

Secondary PK outcome variables

End point type	Secondary

End point timeframe:

10 minutes after achieving target concentration

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: µg/ml				
median (inter-quartile range (Q1-Q3))	4.45 (3.5 to 5.6)	4.3 (3.5 to 6.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Propofol Concentration 30 minutes after achieving target concentration

End point title	Plasma Propofol Concentration 30 minutes after achieving target concentration

End point description:

Secondary PK outcome variables

End point type	Secondary

End point timeframe:

30 minutes after achieving target concentration

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: µg/ml				
median (inter-quartile range (Q1-Q3))	4.45 (3.3 to 5.8)	4.35 (3.4 to 5.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum percent change in mean arterial pressure (MAP) from Baseline to Time of LOER

End point title	Maximum percent change in mean arterial pressure (MAP) from Baseline to Time of LOER

End point description:

MAP = DBP + (SBP - DBP)/3 rounded to the nearest integer, where SBP = systolic blood pressure and DBP = diastolic blood pressure.
Baseline is defined as the last non-missing measurement taken prior to the initiation of study drug infusion.
The first MAP measurement after LOER was considered as the value at LOER.

End point type	Secondary

End point timeframe:

From baseline to time of LOER

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33[5]	35[6]		
Units: Percent				
arithmetic mean (standard deviation)	-9.39 (± 14.622)	-7.09 (± 17.167)		

Notes:

[5] - Safety analysis set

[6] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum percent change in heart rate from Baseline to Time of LOER

End point title	Maximum percent change in heart rate from Baseline to Time of LOER

End point description:

Baseline is defined as the last non-missing measurement taken prior to the initiation of study drug infusion. Heart rate (beats/minute) was based on the measurement of pulse rate.
The first pulse rate measurement after LOER was considered as the value of heart rate at time of LOER.

End point type	Secondary

End point timeframe:

From baseline to time of LOER

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	35		
Units: Percent				
arithmetic mean (standard deviation)	-4.99 (± 13.434)	-3.62 (± 15.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Score for Facial Expression 1 min after start of infusion

End point title	Pain Score for Facial Expression 1 min after start of infusion

End point description:

Pain score of facial expression: Score 0 - if the subject has a relaxed face, makes eye contact, shows interest in surroundings; Score 1 - if the subject has a worried facial expression, with eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed; Score 2 - if the subject has deep furrows in the forehead, closed eyes, an open mouth, deep lines around nose and lips.

End point type	Secondary

End point timeframe:

1 min after start of infusion

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Number of subjects with available result				
Score 0	22	16		
Score 1	9	7		
Score 2	3	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Score for Facial Expression 6 min after start of infusion

End point title	Pain Score for Facial Expression 6 min after start of infusion

End point description:

Pain score of facial expression: Score 0 - if the subject has a relaxed face, makes eye contact, shows interest in surroundings; Score 1 - if the subject has a worried facial expression, with eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed; Score 2 - if the subject has deep furrows in the forehead, closed eyes, an open mouth, deep lines around nose and lips.

End point type	Secondary

End point timeframe:

6 min after start of infusion

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Number of subjects with available result				

Score 0	1	1		
Score 1	0	0		
Score 2	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Score for Motor Response to Light Pressure 1 min after start of infusion

End point title	Pain Score for Motor Response to Light Pressure 1 min after start of infusion

End point description:

Pain score of motor response to light pressure at site of or proximal to venous cannula where the study drug was infused: Score 0 - if there is no response; Score 1 - if the subject withdraws or guards the infusion site; Score 2 - if spontaneous motor response (withdraws or guards the injection without light pressure).

End point type	Secondary

End point timeframe:

1 min after start of infusion

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Number of subjects with available result				
Score 0	23	13		
Score 1	4	11		
Score 2	7	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Score for Motor Response to Light Pressure 6 min after start of infusion

End point title	Pain Score for Motor Response to Light Pressure 6 min after start of infusion

End point description:

Pain score of motor response to light pressure at site of or proximal to venous cannula where the study drug was infused: Score 0 - if there is no response; Score 1 - if the subject withdraws or guards the infusion site; Score 2 - if spontaneous motor response (withdraws or guards the injection without light pressure).

End point type	Secondary

End point timeframe:

6 min after start of infusion

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Number of subjects with available result				
Score 0	0	1		
Score 1	1	0		
Score 2	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Score for Verbal Response 1 min after start of infusion

End point title	Pain Score for Verbal Response 1 min after start of infusion

End point description:

Pain score of verbal response to light pressure at site of or proximal to venous cannula where the study drug was infused : Score 0 - if there is no verbal response; Score 1 - if the subject makes any sound or verbalisation; Score 2 - if spontaneous verbal expression of pain (without light pressure).

End point type	Secondary

End point timeframe:

1 min after start of infusion

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Number of subjects with available result				
Score 0	16	13		
Score 1	7	6		
Score 2	11	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain Score for Verbal Response 6 min after start of infusion

End point title	Pain Score for Verbal Response 6 min after start of infusion

End point description:

Pain score of verbal response to light pressure at site of or proximal to venous cannula where the study drug was infused: Score 0 - if there is no verbal response; Score 1 - if the subject makes any sound or verbalisation; Score 2 - if spontaneous verbal expression of pain (without light pressure).

End point type	Secondary

End point timeframe:

6 min after start of infusion

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Number of subjects with available result				
Score 0	1	1		
Score 1	0	0		
Score 2	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Spontaneous Eye Opening

End point title	Time to Spontaneous Eye Opening

End point description:

Time to eye opening (minutes) was derived based on the time of eye opening relative to termination time of study drug infusion. Time to spontaneous eye opening (minutes) = (date/time of spontaneous eye opening – date/time of termination of study drug infusion).

End point type	Secondary

End point timeframe:

From termination of study drug infusion until spontaneous eye opening

End point values	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Minutes				
arithmetic mean (standard deviation)	24.7 (± 11.87)	19.7 (± 12.84)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period of observation lasted from the day the patient signed the Informed Consent until the last follow-up visit. The Investigator had to report any SAE without undue delay within 24 hours following first awareness of the event.

Adverse event reporting additional description:

In this study, all AEs/SAEs were documented, but only treatment-emergent adverse events (TEAEs), i.e. AEs that started or worsened in severity at or after the initiation of study drug infusion till the end of the study, including the Follow-up Visit, were reported and summarized in tables.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Propofol 2% (20 mg/mL) MCT Fresenius
Reporting group description: -	
Reporting group title	Diprivan 20 mg/mL (AstraZeneca)

Reporting group description: -

Serious adverse events	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Propofol 2% (20 mg/mL) MCT Fresenius	Diprivan 20 mg/mL (AstraZeneca)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 35 (88.57%)	31 / 35 (88.57%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	9 / 35 (25.71%)	4 / 35 (11.43%)	
occurrences (all)	9	4	
Haematoma			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Hyperthermia			
subjects affected / exposed	3 / 35 (8.57%)	4 / 35 (11.43%)	
occurrences (all)	3	4	
Fatigue			
subjects affected / exposed	4 / 35 (11.43%)	1 / 35 (2.86%)	
occurrences (all)	4	1	
Infusion site pain			
subjects affected / exposed	2 / 35 (5.71%)	2 / 35 (5.71%)	
occurrences (all)	2	2	
Injection site pain			
subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)	
occurrences (all)	1	3	
Malaise			
subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)	
occurrences (all)	1	3	
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Asthenia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Hypothermia			

subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Injection site haematoma			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Immune system disorders			
Iodine allergy			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Penile pain			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 35 (2.86%)	2 / 35 (5.71%)	
occurrences (all)	1	2	
Agitation			
subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
occurrences (all)	1	1	
Depression			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Investigations			
C-reactive protein increased			

subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Blood pressure increased			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Blood urine			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Blood urine present			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Oxygen saturation decreased			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Respiratory rate decreased			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	10 / 35 (28.57%)	13 / 35 (37.14%)	
occurrences (all)	10	13	
Post procedural swelling			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Wound complication			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Bradycardia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
occurrences (all)	1	1	
Syncope			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Presyncope			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 35 (5.71%)	3 / 35 (8.57%)	
occurrences (all)	2	3	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	8 / 35 (22.86%)	8 / 35 (22.86%)	
occurrences (all)	8	8	
Nausea			
subjects affected / exposed	7 / 35 (20.00%)	6 / 35 (17.14%)	
occurrences (all)	7	6	
Vomiting			
subjects affected / exposed	5 / 35 (14.29%)	5 / 35 (14.29%)	
occurrences (all)	5	5	
Constipation			
subjects affected / exposed	2 / 35 (5.71%)	3 / 35 (8.57%)	
occurrences (all)	2	3	
Abdominal Pain			
subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
occurrences (all)	1	1	
Diarrhoea			

subjects affected / exposed	2 / 35 (5.71%)	0 / 35 (0.00%)	
occurrences (all)	2	0	
Abdominal distension			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Abdominal hernia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Gastrointestinal disorder			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
occurrences (all)	1	1	
Cold sweat			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Urinary retention			

subjects affected / exposed	1 / 35 (2.86%)	1 / 35 (2.86%)	
occurrences (all)	1	1	
Dysuria			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 35 (5.71%)	3 / 35 (8.57%)	
occurrences (all)	2	3	
Neck pain			
subjects affected / exposed	1 / 35 (2.86%)	4 / 35 (11.43%)	
occurrences (all)	1	4	
Pain in extremity			
subjects affected / exposed	1 / 35 (2.86%)	3 / 35 (8.57%)	
occurrences (all)	1	3	
Musculoskeletal pain			
subjects affected / exposed	2 / 35 (5.71%)	1 / 35 (2.86%)	
occurrences (all)	2	1	
Arthralgia			
subjects affected / exposed	0 / 35 (0.00%)	2 / 35 (5.71%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 35 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 35 (0.00%)	1 / 35 (2.86%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Only a descriptive comparison of the primary endpoint (time to LOER) between test and reference treatment was performed. Therefore, no statistical inference was taken.

Notes: