Clinical trial results:
Propofol and etomidate.
Are they also safe for patients with Brugada-Syndrome?

Summary

EudraCT number	2012-000584-25
Trial protocol	BE
Global end of trial date	31 March 2018

Results information

Result version number	v1 (current)
This version publication date	21 May 2021
First version publication date	21 May 2021
Summary attachment (see zip file)	Published Article of Study (PACE Safe Single Dose Propofol Administration in patients with established Brugada Syndrome. A Retrospective Database Analysis.pdf)

Trial information

Trial identification

Sponsor protocol code	FLAM01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UZ Brussels
Sponsor organisation address	Laarbeeklaan 101, Brussels, Belgium, 1090
Public contact	Anaesthesia Department, UZBrussel, 0032 24778926, panagiotis.flamee@me.com
Scientific contact	Anaesthesia Department, UZBrussel, 0032 24778926, panagiotis.flamee@me.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	19 April 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to investigate whether commonly used hypnotic agents, propofol and etomidate, are also safe for patients with BrS.

Protection of trial subjects:

The implantation was performed under general anesthesia. We reviewed the anesthetic chart of each patient investigating the occurrence of malignant arrhythmic events and the need for defibrillation during induction and maintenance of anesthesia. The choice of hypnotic agent and the dose administered for induction of anesthesia were registered. General anesthesia was conducted in an operating theater where an external cardioverter defibrillator was attached to the patient with adhesive pads prior to the procedure. The radial artery was cannulated for invasive blood pressure monitoring. Further monitoring of the patient comprised five-lead ECG, pulse oxymetry, and continuous carbon dioxide monitoring through side sampling from the ventilator tubes. Anesthesia was induced with propofol and sufentanyl. The airway was secured with a laryngeal mask or an endotracheal tube. In the latter, a muscle relaxant was administered in addition. Injection of propofol occurred in a single shot bolus—as often performed by most anesthetists—over a few seconds. Anesthesia was maintained with volatile anesthetics (sevoflurane or desflurane) in an oxygen-air mixture. Nitrous oxide was not used in this study. AICD implantation was performed by a cardiac surgeon via a nonthoracotomy transvenous lead system. Upon successful implantation of the AICD, defibrillation threshold testing was conducted and the wound was sutured. No local anesthetics were further administered.
Statistics
In this study, descriptive st

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2012
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	Belgium: 57
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	3
Adolescents (12-17 years)	2
Adults (18-64 years)	48
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Since 1996, all patients diagnosed with BS and their relatives tested for the syndrome have been included in a registry and followed-up in a prospective fashion. BS was diagnosed clinically according to the modified task force criteria. Extended retrospective analysis of 429 patients with BS from the aforementioned database
was performed.

Pre-assignment

Screening details:

During screening patients were checked if they had been diagnosed with Brugada Syndrome. An ECG would be taken and analysed by 3 cardiologist to determine if they had coved-type ST-segment elevation in the right precordial leads.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Group A

Arm description:

Propofol is an anesthetic drug with a very attractive pharmacokinetic profile, which makes it the induction agent of choice, especially in day-case surgery. Data on its potential proarrhythmic effects in patients with Brugada syndrome (BS) patients are still lacking. The aim of our study was to investigate whether a single dose of propofol triggered any adverse events in consecutive high-risk patients with BS. All consecutive patients with BS having undergone an implantable cardiac defibrillator implantation under general anesthesia were eligible for this study. The anesthetic chart of each patient was reviewed, and the occurrence of malignant arrhythmic events as well as the need for defibrillation during induction and maintenance of anesthesia was investigated. Further monitoring of the patient comprised five-lead electrocardiogram (ECG), pulse oxymetry, and continuous carbon dioxide monitoring through side sampling from the ventilator tubes.

Arm type	Standard therapy
Investigational medicinal product name	Propofol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

dose ranged between 0.8 mg/kg and 5.0 mg/kg

Investigational medicinal product name	sufentanyl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

0.5% - 8% via oxygen mask

Number of subjects in period 1	Group A
Started	57
Completed	57

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	57	57	
Age categorical			
Patients ranging van 6 years old till 85 years old.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	3	3	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	48	48	
From 65-84 years	4	4	
85 years and over	0	0	
All patients	0	0	
Gender categorical			
All genders			
Units: Subjects			
Female	22	22	
Male	35	35	

End points

End points reporting groups

Reporting group title	Group A

Reporting group description:

Propofol is an anesthetic drug with a very attractive pharmacokinetic profile, which makes it the induction agent of choice, especially in day-case surgery. Data on its potential proarrhythmic effects in patients with Brugada syndrome (BS) patients are still lacking. The aim of our study was to investigate whether a single dose of propofol triggered any adverse events in consecutive high-risk patients with BS. All consecutive patients with BS having undergone an implantable cardiac defibrillator implantation under general anesthesia were eligible for this study. The anesthetic chart of each patient was reviewed, and the occurrence of malignant arrhythmic events as well as the need for defibrillation during induction and maintenance of anesthesia was investigated. Further monitoring of the patient comprised five-lead electrocardiogram (ECG), pulse oxymetry, and continuous carbon dioxide monitoring through side sampling from the ventilator tubes.

Primary: Number of arrhythmias

End point title	Number of arrhythmias[1]

End point description:

End point type	Primary

End point timeframe:

Hours during operation

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were used and values are reported in mean +- standard deviation. In case of proportions, the absolute numbers were reported followed by percentages. There was no statistical test performed between to groups.

End point values	Group A			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: number of arrhytmias	57			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

For maximum a week post operation. Until hospital discharge.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Total group

Reporting group description: -

Serious adverse events	Total group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 57 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Total group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 57 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No patient developed a malignant rhythm during induction and maintenance of anesthesia. All patients were then safely discharged from the postanesthetic care unit after 1 hour. No adverse events were noticed during the recovery phase. Subsequent to 24 hours of monitoring, patients left the hospital in good condition.

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

None reported