



Clinical trial results:

Comparison between Propofol and Inhalational Anaesthetic Agents on Cardiovascular Outcomes following Cardiac Surgery - a Randomised Controlled Feasibility Trial

Summary

EudraCT number	2019-000171-16
Trial protocol	GB
Global end of trial date	11 May 2022

Results information

Result version number	v1 (current)
This version publication date	03 May 2026
First version publication date	03 May 2026
Summary attachment (see zip file)	COPIA CSR (CSR COPIA v1.0 Final.pdf)

Trial information

Trial identification

Sponsor protocol code	KCH-PRO:19/001
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	King's College Hospital NHS Foundation Trust
Sponsor organisation address	Great Maze Pond, London, United Kingdom, SE1 9RT
Public contact	Dr Gudrun Kunst, King's College Hospital NHS Foundation Trust, 44 02032993154 , gudrun.kunst@kcl.ac.uk
Scientific contact	Dr Gudrun Kunst, King's College Hospital NHS Foundation Trust, 44 02032993154 , gudrun.kunst@kcl.ac.uk

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	16 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 November 2021
Global end of trial reached?	Yes
Global end of trial date	11 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the COPIA feasibility trial is to determine feasibility of the proposed multicentre study:

1. Determination of the likely rate of recruitment at two centres.
2. Identification of potential recruitment barriers with current protocol.

Protection of trial subjects:

Participants have the right to withdraw from the study at any time for any reason. The investigator also has the right to withdraw patients from the study drug in the event of inter-current illness, AEs, SAEs, SUSARs, protocol violations, cure, administrative reasons or other reasons. It is understood by all concerned that an excessive rate of withdrawals can render the study un-interpretable; therefore, unnecessary withdrawal of patients should be avoided. Should a patient decide to withdraw from the study, all efforts will be made to report the reason for withdrawal as thoroughly as possible. Should a patient withdraw from study drug only, efforts will be made to continue to obtain follow-up data, with the permission of the patient. A patient may decide to withdraw from the trial at any time without prejudice to their future care.

Background therapy:

Myocardial revascularisation and cardiopulmonary bypass (CPB) can cause ischaemia-reperfusion injury, leading to myocardial and other end-organ damage. Volatile anaesthetics protect the myocardium in experimental studies. However, there is uncertainty about whether this translates into clinical benefits because of the coadministration of propofol and its detrimental effects, restricting myocardial protective processes.

In summary, the proposed feasibility trial will, for the first time, compare volatile anaesthetics as the only anaesthetic agent (without propofol), with the administration of propofol only for maintenance of anaesthesia and investigate meaningful clinical outcomes. The results of the feasibility trial will be used to assess whether it is clinically acceptable and achievable to compare propofol anaesthesia with inhalational anaesthesia as the induction and maintenance agent during cardiac surgery.

Evidence for comparator: -

Actual start date of recruitment	01 July 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 50
Worldwide total number of subjects	50
EEA total number of subjects	0

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)	15
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	416 ^[1]
Number of subjects completed	50

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Ineligible: 308
Reason: Number of subjects	Eligible but declined consent: 58

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: We do not count screening participants as enrolled

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

Staff at each site, and at the LSHTM CTU, will be arranged into blinded and unblinded teams. This will be recorded in the delegation log at each organisation. For the duration of the trial, staff may move from the blinded team to the unblinded team, but not from the unblinded team to the blinded team.

Arms

Are arms mutually exclusive?	Yes
Arm title	Volatile group

Arm description:

Volatile anaesthetics, either isoflurane, sevoflurane or desflurane, used for maintenance of anaesthesia. Administration via inhalation / ventilation through alveolar membrane in lungs. The maintenance dose of the volatile anaesthetic agent will be titrated to doses deemed necessary in order to provide sufficient depth of anaesthesia and blood pressure.

Arm type	Experimental
Investigational medicinal product name	Volatile anaesthetic agents
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation vapour, solution
Routes of administration	Inhalation use

Dosage and administration details:

The volatile anaesthetic agent was administered via inhalation, i.e. ventilation through alveolar membrane in lungs, for induction and during the maintenance of anaesthesia. During CPB the volatile anaesthetic agent was administered through the oxygenator oxygen inflow of the CPB machine. The maintenance dose of the volatile anaesthetic agent was titrated to doses deemed necessary in order to provide sufficient depth of anaesthesia (titrated to a depth of anaesthesia with an approximate BIS of 30-60) and mean arterial pressure (MAP) of 50-80mmHg by the treating anaesthetist.

The administration of the volatile anaesthetic agent was started with the induction of anaesthesia and ended at the end of surgery, before the patient transferred to the CCU.

Arm title	Propofol group
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Arm description:

Propofol, an intravenous anaesthetic used for maintenance of anaesthesia. The maintenance dose of the propofol infusion will be titrated to doses deemed necessary in order to provide sufficient depth of anaesthesia without blood pressure.

Arm type	Active comparator
Investigational medicinal product name	Propofol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Propofol was administered via an infusion. Patients received propofol only during the surgical procedure. The maintenance dose of the propofol infusion was titrated to doses deemed necessary in order to provide sufficient depth of anaesthesia (titrated to a depth of anaesthesia with an approximate BIS of 30-60) and mean arterial pressure (MAP) of 50-80mmHg by the treating anaesthetist.

Number of subjects in period 1	Volatile group	Propofol group
Started	25	25
Completed	22	22
Not completed	3	3
Consent withdrawn by subject	-	1
Died before discharge	1	-
Died after discharge	1	1
Incomplete dataset	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	50	50	
Age categorical			
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	15	15	
From 65-84 years	34	34	
85 years and over	0	0	
Not recorded	1	1	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	38	38	
Not recorded	1	1	
Ethnicity			
Units: Subjects			
White	44	44	
Black	1	1	
Asian	2	2	
Missing data	3	3	

End points

End points reporting groups

Reporting group title	Volatile group
Reporting group description: Volatile anaesthetics, either isoflurane, sevoflurane or desflurane, used for maintenance of anaesthesia. Administration via inhalation / ventilation through alveolar membrane in lungs. The maintenance dose of the volatile anaesthetic agent will be titrated to doses deemed necessary in order to provide sufficient depth of anaesthesia and blood pressure.	
Reporting group title	Propofol group
Reporting group description: Propofol, an intravenous anaesthetic used for maintenance of anaesthesia. The maintenance dose of the propofol infusion will be titrated to doses deemed necessary in order to provide sufficient depth of anaesthesia without blood pressure.	

Primary: Protocol adherence

End point title	Protocol adherence ^[1]
End point description:	
End point type	Primary
End point timeframe: From screening to 30-day follow-up	
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: Please see uploaded report	

End point values	Volatile group	Propofol group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: protocol violations				
Not recorded	1	1		
Protocol violation	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Median time at the time point of the 30-day follow-up

End point title	Median time at the time point of the 30-day follow-up
End point description:	
End point type	Secondary
End point timeframe: Surgery to 30-day follow-up	

End point values	Volatile group	Propofol group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 ^[2]	22 ^[3]		
Units: days				
arithmetic mean (full range (min-max))				
Median time	33 (30 to 54)	37.5 (31 to 49)		

Notes:

[2] - 1 patient did not have surgery, 1 patient died before discharge and 1 patient died after discharge

[3] - 1 patient withdrew consent before surgery, 1 died after discharge, 1 had incomplete data set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From day of surgery to 30 days post-randomisation

Assessment type	Systematic
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Dictionary used

Dictionary name	Not specified in CSR
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Dictionary version	N/A
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Reporting groups

Reporting group title	Volatile group
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Reporting group description: -

Reporting group title	Propofol group
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Reporting group description: -

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: According to the CSR, there were no non-serious AEs. Please see report.

Serious adverse events	Volatile group	Propofol group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
number of deaths (all causes)	3	2	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 1	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	Volatile group	Propofol group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 2020	SA001 Protocol v2.0 22 January 2020
23 March 2022	SA002 RSI update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported