



## Clinical trial results:

### Determination of the optimal dose of ephedrine to treat hypotension during surgery of newborn to six months infant

#### Summary

EudraCT number	2014-004190-16
Trial protocol	FR
Global end of trial date	05 September 2020

#### Results information

Result version number	v1 (current)
This version publication date	13 December 2025
First version publication date	13 December 2025

#### Trial information

##### Trial identification

Sponsor protocol code	69HCL14-0248
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02384876
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Hospices Civils de Lyon
Sponsor organisation address	3 Quai des Célestins, Lyon, France, 69002
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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	21 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 September 2020
Global end of trial reached?	Yes
Global end of trial date	05 September 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the optimal dose of ephedrine (in mg/kg) to be used as a first-line, in single administration, in intraoperative arterial hypotension of newborns and infants up to six months of age

Protection of trial subjects:

The trial was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

A safety monitoring committee was established before the start of the trial. Recommendations were given on the continuation of the study between each cohort and at each occurrence of a serious adverse event.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2015
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	France: 119
Worldwide total number of subjects	119
EEA total number of subjects	119

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	8
Infants and toddlers (28 days-23 months)	111
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

All patients meeting the eligibility criteria and admitted to the pediatric anesthesia departments headed by Prof. Chassard (Hôpital Femme Mère Enfant, Hospices Civils de Lyon), Prof. Bazin (Hôpital Estaing, CHU Clermont Ferrand) and Prof. Moliex (Hôpital Nord, CHU Saint-Etienne) were proposed participation in the trial.

### Pre-assignment

Screening details:

All patients meeting the eligibility criteria and admitted to the pediatric anesthesia departments headed by Prof. Chassard (Hôpital Femme Mère Enfant, Hospices Civils de Lyon), Prof. Bazin (Hôpital Estaing, CHU Clermont Ferrand) and Prof. Moliex (Hôpital Nord, CHU Saint-Etienne) were proposed participation in the trial.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Ephedrine 0.1 mg/kg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ephedrine 30mg/100mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

single administration in case of hypotension at the anesthesia induction.

<b>Arm title</b>	Ephedrine 0.6 mg/kg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ephedrine 30mg/100mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

single administration in case of hypotension at the anesthesia induction.

<b>Arm title</b>	Ephedrine 0.8 mg/kg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ephedrine 30mg/100mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

single administration in case of hypotension at the anesthesia induction.

<b>Arm title</b>	Ephedrine 1 mg/kg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Ephedrine 30mg/100mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

single administration in case of hypotension at the anesthesia induction.

<b>Arm title</b>	Ephedrine 1.2 mg/kg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Ephedrine 30mg/100mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

single administration in case of hypotension at the anesthesia induction.

<b>Arm title</b>	Ephedrine 1.4 mg/kg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Ephedrine 30mg/100mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

single administration in case of hypotension at the anesthesia induction.

<b>Number of subjects in period 1</b>	Ephedrine 0.1 mg/kg	Ephedrine 0.6 mg/kg	Ephedrine 0.8 mg/kg
Started	24	24	21
Completed	24	24	21

<b>Number of subjects in period 1</b>	Ephedrine 1 mg/kg	Ephedrine 1.2 mg/kg	Ephedrine 1.4 mg/kg
Started	17	16	17
Completed	17	16	17



## Baseline characteristics

### Reporting groups

Reporting group title	Ephedrine 0.1 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 0.6 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 0.8 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1.2 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1.4 mg/kg
Reporting group description: -	

Reporting group values	Ephedrine 0.1 mg/kg	Ephedrine 0.6 mg/kg	Ephedrine 0.8 mg/kg
Number of subjects	24	24	21
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	1	1	2
Infants and toddlers (28 days-23 months)	23	23	19
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	9	2	7
Male	15	22	14

Reporting group values	Ephedrine 1 mg/kg	Ephedrine 1.2 mg/kg	Ephedrine 1.4 mg/kg
Number of subjects	17	16	17
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	1	2	1
Infants and toddlers (28 days-23 months)	16	14	16
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0

From 65-84 years	0	0	0
85 years and over	0	0	0

Gender categorical Units: Subjects			
Female	3	5	4
Male	14	11	13

<b>Reporting group values</b>	Total		
Number of subjects	119		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	8		
Infants and toddlers (28 days-23 months)	111		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Gender categorical Units: Subjects			
Female	30		
Male	89		

### Subject analysis sets

Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:

all patients who were randomized and who received the treatment

<b>Reporting group values</b>	Per Protocol Set		
Number of subjects	119		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	8		
Infants and toddlers (28 days-23 months)	111		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		



Gender categorical			
Units: Subjects			
Female	30		
Male	89		

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## End points

### End points reporting groups

Reporting group title	Ephedrine 0.1 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 0.6 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 0.8 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1.2 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1.4 mg/kg
Reporting group description: -	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description:	
all patients who were randomized and who received the treatment	

### Primary: Percentage of success

End point title	Percentage of success
End point description:	
The primary outcome was defined as a MAP greater than 80% of the baseline MAP within 10 minutes post ephedrine administration. Another infusion of ephedrine or the administration of dopamine or adrenaline, or a vascular filling, within 10 minutes after the initial dose of ephedrine were considered as a failure. Baseline MAP was the mean of two MAP recorded before anaesthetic induction	
End point type	Primary
End point timeframe:	
10 minutes	

End point values	Ephedrine 0.1 mg/kg	Ephedrine 0.6 mg/kg	Ephedrine 0.8 mg/kg	Ephedrine 1 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	24	21	17
Units: Events	3	7	8	8

End point values	Ephedrine 1.2 mg/kg	Ephedrine 1.4 mg/kg	Per Protocol Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	16	17	119	
Units: Events	9	7	42	

## Statistical analyses

<b>Statistical analysis title</b>	Logistic regression model, adjusted on the cohort
Comparison groups	Ephedrine 0.6 mg/kg v Ephedrine 0.1 mg/kg
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other <sup>[1]</sup>
Parameter estimate	NA
Point estimate	13.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	35.4

Notes:

[1] - precision of the estimate

<b>Statistical analysis title</b>	Logistic regression model, adjusted on the cohort
Comparison groups	Ephedrine 0.8 mg/kg v Ephedrine 0.1 mg/kg
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other <sup>[2]</sup>
Parameter estimate	NA
Point estimate	32.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	59.1

Notes:

[2] - precision of the estimate

<b>Statistical analysis title</b>	Logistic regression model, adjusted on the cohort
Comparison groups	Ephedrine 1 mg/kg v Ephedrine 0.1 mg/kg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other <sup>[3]</sup>
Parameter estimate	NA
Point estimate	37.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.9
upper limit	67.2

Notes:

[3] - precision of the estimate

<b>Statistical analysis title</b>	Logistic regression model, adjusted on the cohort
Comparison groups	Ephedrine 1.2 mg/kg v Ephedrine 0.1 mg/kg

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other <sup>[4]</sup>
Parameter estimate	NA
Point estimate	56.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.7
upper limit	80.2

Notes:

[4] - precision of the estimate

<b>Statistical analysis title</b>	Logistic regression model, adjusted on the cohort
Comparison groups	Ephedrine 1.4 mg/kg v Ephedrine 0.1 mg/kg
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other <sup>[5]</sup>
Parameter estimate	NA
Point estimate	31.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	63.9

Notes:

[5] - precision of the estimate

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Continuous AE reporting from randomization (day of general anesthesia) to end of participation (hospitalization time ; three days max).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	xx

### Reporting groups

Reporting group title	Ephedrine 0.1 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 0.6 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 0.8 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1.2 mg/kg
Reporting group description: -	
Reporting group title	Ephedrine 1.4 mg/kg
Reporting group description: -	

Serious adverse events	Ephedrine 0.1 mg/kg	Ephedrine 0.6 mg/kg	Ephedrine 0.8 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	1 / 21 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Pseudomeningocele			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound complication			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Absence seizure			

subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fever			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia coli infection			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Ephedrine 1 mg/kg	Ephedrine 1.2 mg/kg	Ephedrine 1.4 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Pseudomeningocele			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Absence seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Fever			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Escherichia coli infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Ephedrine 0.1 mg/kg	Ephedrine 0.6 mg/kg	Ephedrine 0.8 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	0 / 21 (0.00%)
Injury, poisoning and procedural complications			
Administration error at the time of ephedrine injection			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Digestive pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
DIARRHEA			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary globe			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
HEMATURIA			

subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	1 / 24 (4.17%) 1	0 / 21 (0.00%) 0
Metabolism and nutrition disorders HYPOVOLEMIA subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0	0 / 24 (0.00%) 0	0 / 21 (0.00%) 0

<b>Non-serious adverse events</b>	Ephedrine 1 mg/kg	Ephedrine 1.2 mg/kg	Ephedrine 1.4 mg/kg
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 17 (17.65%)	3 / 16 (18.75%)	0 / 17 (0.00%)
Injury, poisoning and procedural complications Administration error at the time of ephedrine injection subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0
Gastrointestinal disorders Digestive pain subjects affected / exposed occurrences (all)  DIARRHEA subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0  0 / 17 (0.00%) 0  1 / 17 (5.88%) 1	1 / 16 (6.25%) 1  1 / 16 (6.25%) 1  0 / 16 (0.00%) 0	0 / 17 (0.00%) 0  0 / 17 (0.00%) 0  0 / 17 (0.00%) 0
Renal and urinary disorders Urinary globe subjects affected / exposed occurrences (all)  HEMATURIA subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1  0 / 17 (0.00%) 0	0 / 16 (0.00%) 0  0 / 16 (0.00%) 0	0 / 17 (0.00%) 0  0 / 17 (0.00%) 0
Metabolism and nutrition disorders HYPOVOLEMIA subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0





## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2015	change of coordinating investigator and eligibility criteria
30 May 2017	change of coordinating investigator+ extension of the recruitment period
21 May 2019	extension of the recruitment period and implementation of GPRD
09 June 2020	extension of the recruitment period

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 March 2020	COVID period	19 June 2020

Notes:

### Limitations and caveats

None reported