Clinical trial results:
Comparison of the efficacy of ephedrine versus norepinephrine in the treatment of hypotension occurring after induction of general anesthesia in patients with chronic renal failure: randomized double-blind pilot study

Summary

EudraCT number	2022-002892-12
Trial protocol	BE
Global end of trial date	27 July 2023

Results information

Result version number	v1 (current)
This version publication date	21 July 2024
First version publication date	21 July 2024

Trial information

Trial identification

Sponsor protocol code	CHUB-VASO-IRC

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CHU Brugmann
Sponsor organisation address	4 Place Arthur Van Gehuchten , Brussels, Belgium, 1020
Public contact	Anesthesiology Department, CHU Brugmann, 32 24775676, zakaria.cheffi@chu-brugmann.be
Scientific contact	Anesthesiology Department, CHU Brugmann, 32 24775676, zakaria.cheffi@chu-brugmann.be

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	27 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 July 2023
Global end of trial reached?	Yes
Global end of trial date	27 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main aim of this study is to compare the efficacy of ephedrine versus norepinephrine in the treatment of hypotension occurring after induction of general anesthesia in patients with chronic renal failure during elective surgery.

Protection of trial subjects:

The risk to which the patient is exposed is the risk linked to general anesthesia. This risk is in practice controlled by the means implemented daily for patients undergoing general anesthesia within the hospital.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2022
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: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	11
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is a monocentric study held within the CHU Brugmann Hospital. Recruitment started on 13 september 2022. The study did not reach its recruitment goal (early termination on 27 July 2023).

Pre-assignment

Screening details:

The study was offered to all patients of the CHU Brugmann Hospital with chronic renal failure either during the anesthesia consultation or during the pre-anesthetic visit in the room.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Noradrenalin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Noradrenaline tartate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

The patient receives a bolus of 2ml of noradrenalin 3µg/ml every 3 minutes if he/she is hypotensive, until the blood pressure is above the set thresholds (mean arterial pressure (MAP) >65 mmHg).

Arm title	Ephedrin

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ephedrine hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intravenous bolus use

Dosage and administration details:

The patient receives a bolus of 2 ml of ephedrine 3 mg/ml every 3 minutes if he/she is hypotensive, until the blood pressure is above the set thresholds (mean arterial pressure (MAP) >65 mmHg).

Number of subjects in period 1	Noradrenalin	Ephedrin
Started	12	12
Completed	8	9
Not completed	4	3
Adverse event, serious fatal	1	-
Consent withdrawn by subject	2	-
Not randomized	-	1
Lost to follow-up	-	1
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Noradrenalin
Reporting group description: -	
Reporting group title	Ephedrin
Reporting group description: -	

Reporting group values	Noradrenalin	Ephedrin	Total
Number of subjects	12	12	24
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	6	11
From 65-84 years	7	6	13
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	4	2	6
Male	8	10	18

End points

End points reporting groups

Reporting group title	Noradrenalin
Reporting group description: -	
Reporting group title	Ephedrin
Reporting group description: -	

Primary: Amount of boluses to maintain a mean arterial pressure >65mmHg

End point title	Amount of boluses to maintain a mean arterial pressure >65mmHg[1]
End point description:	
End point type	Primary
End point timeframe:	
From the start of the surgical procedure until the first parameter measurement in the post-intervention monitoring room.	
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: The trial ended prematurely without reaching its recruitment goal. It makes no sense to perform statistics on such a small patient sample.	

End point values	Noradrenalin	Ephedrin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: N/A				
median (inter-quartile range (Q1-Q3))	0.5 (0 to 4.25)	0 (0 to 3)		

Statistical analyses

No statistical analyses for this end point

Primary: Mean arterial pressure (MAP) during intervention

End point title	Mean arterial pressure (MAP) during intervention[2]
End point description:	
End point type	Primary
End point timeframe:	
From the start of the surgical procedure until the first parameter measurement in the post-intervention monitoring room.	
Notes:	
[2] - 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: The trial ended prematurely without reaching its recruitment goal. It makes no sense to perform statistics on such a small patient sample.	

End point values	Noradrenalin	Ephedrin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: mmHg				
median (inter-quartile range (Q1-Q3))	88 (79.75 to 99.25)	87 (73 to 92)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Entire trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Noradrenalin
Reporting group description: -	
Reporting group title	Ephedrin
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: The study team confirmed no non-serious AE occurred.

Serious adverse events	Noradrenalin	Ephedrin	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Noradrenalin	Ephedrin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2022	- Modifications in inclusion/exclusion criteria (age extended to 75 years, BMI limit 35) - Modifications in the 'standard of care' procedure for anesthesia (details on the hypnotic and curarizing agents) - Change in co-investigators

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 July 2023	Premature end of trial	-

Notes:

Limitations and caveats

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

Methodological issue: in order to have significant results, 360 patients (180 per group) would be needed (instead of the 60 foreseen by the protocol). This is not feasible in our hospital setting.

Notes: