



Clinical trial results:

Neuroprotective goal directed hemodynamic optimization in post-cardiac arrest patients: a randomized controlled trial (the NEUROPROTECT post-CA trial)

Summary

EudraCT number	2015-002151-10
Trial protocol	BE
Global end of trial date	30 June 2018

Results information

Result version number	v1 (current)
This version publication date	20 March 2024
First version publication date	20 March 2024

Trial information

Trial identification

Sponsor protocol code	NEUROPROTECTpost-CA
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02541591
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospitals Leuven (UZ Leuven)
Sponsor organisation address	Herestraat 49, Leuven, Belgium, 3000
Public contact	Stefan Janssens, UZ Leuven, 32 16344246, stefan.janssens@uzleuven.be
Scientific contact	Stefan Janssens, UZ Leuven, 32 16344246, stefan.janssens@uzleuven.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	30 June 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial is to assess whether or not a new goal directed hemodynamic optimization strategy can reduce cerebral ischemia in post-cardiac arrest (CA) patients as quantified by the apparent diffusion coefficient (ADC) on diffusion weighted MRI (DW-MRI) to be performed at day 4-5 post-CA using ADC scores in 11 pre-specified brain regions (frontal cortex, parietal cortex, temporal cortex, occipital cortex, precentral cortex, postcentral cortex, caudate nucleus, putamen, thalamus, cerebellum, pons)

Protection of trial subjects:

see protocol

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 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	Belgium: 112
Worldwide total number of subjects	112
EEA total number of subjects	112

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)	56
From 65 to 84 years	56
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

- o Out-of-hospital CA of presumed cardiac cause irrespective of the presenting rhythm
- o Unconsciousness (Glasgow coma scale < 8) at hospital admission
- o Age \geq 18 years
- o Sustained return of spontaneous circulation (ROSC) (=when chest compressions have not been required for 20 consecutive minutes)

Pre-assignment

Screening details:

- o Out-of-hospital CA of presumed cardiac cause irrespective of the presenting rhythm
- o Unconsciousness (Glasgow coma scale < 8) at hospital admission
- o Age \geq 18 years
- o Sustained return of spontaneous circulation (ROSC) (=when chest compressions have not been required for 20 consecutive minutes)

Period 1

Period 1 title	Overall trial (Baseline - day 4-5) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Neuroprotect

Arm description:

MAP between 85-100mmHg SVO2 between 65-75%

Arm type	neuroprotect
Investigational medicinal product name	inotropes and vasopressors (dobutamine and levophed)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

see protocol

Arm title	Control
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Arm description:

MAP>65mmHg

Arm type	control
Investigational medicinal product name	inotropics and vasopression (dobutamine and levophed)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

see protocol

Number of subjects in period 1 ^[1]	Neuroprotect	Control
Started	52	55
Completed	52	55

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: 4 patients were excluded in the FAS in the neuroprotect group (2 next of kin refused informed consent, and 2 asphyxia as cause of CA)

1 patient was excluded in the FAS in the placebo group (asphyxia as cause of CA)

Baseline characteristics

Reporting groups

Reporting group title	Neuroprotect
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Reporting group description:

MAP between 85-100mmHg SVO2 between 65-75%
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Reporting group title	Control
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Reporting group description:

MAP>65mmHg

Reporting group values	Neuroprotect	Control	Total
Number of subjects	52	55	107
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)	26	27	53
From 65-84 years	26	28	54
85 years and over	0	0	0
Age continuous			
Age continuous			
Units: years			
median	64	65	
standard deviation	± 12	± 13	-
Gender categorical			
gender			
Units: Subjects			
Female	13	13	26
Male	39	42	81

Subject analysis sets

Subject analysis set title	Full analysis
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Subject analysis set type	Full analysis
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Subject analysis set description:

full analysis

Reporting group values	Full analysis		
Number of subjects	107		
Age categorical			
Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	53		
From 65-84 years	54		
85 years and over	0		
Age continuous			
Age continuous			
Units: years			
median	65		
standard deviation	± 12		
Gender categorical			
gender			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Neuroprotect
Reporting group description: MAP between 85-100mmHg SVO2 between 65-75%	
Reporting group title	Control
Reporting group description: MAP>65mmHg	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description: full analysis	

Primary: % of Ischaemic Voxels With an ADC<0.65 mm2/s on Day 4-5 (Diffusion Weighted MRI)

End point title	% of Ischaemic Voxels With an ADC<0.65 mm2/s on Day 4-5 (Diffusion Weighted MRI)
End point description:	
End point type	Primary
End point timeframe: Day 4-5	

End point values	Neuroprotect	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	55		
Units: %				
number (not applicable)	52	55		

Statistical analyses

Statistical analysis title	MI size / LV mass (%)
Comparison groups	Control v Neuroprotect
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0881 ^[1]
Method	ANOVA
Parameter estimate	Median difference (final values)
Point estimate	1.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.98

Notes:

[1] - due to non normality of the residuals the data were log-transformed prior to the anova

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

During study drug treatment (36 hours)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21
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Reporting groups

Reporting group title	Neuroprotect
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Reporting group description:

MAP between 85-100mmHg SVO2 between 65-75%

Reporting group title	Control
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Reporting group description:

MAP>65mmHg

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 non serious adverse events were reported

Serious adverse events	Neuroprotect	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 52 (13.46%)	21 / 52 (40.38%)	
number of deaths (all causes)	31	29	
number of deaths resulting from adverse events			
Vascular disorders			
limb ischemia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 52 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary embolism			
subjects affected / exposed	0 / 52 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac disorders			
Arrhythmia			

subjects affected / exposed	7 / 52 (13.46%)	13 / 52 (25.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 13	
deaths causally related to treatment / all	0 / 4	0 / 6	
Atrial fibrillation			
subjects affected / exposed	0 / 52 (0.00%)	4 / 52 (7.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 3	
Pulmonary congestion			
subjects affected / exposed	0 / 52 (0.00%)	2 / 52 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
death			
subjects affected / exposed	0 / 52 (0.00%)	1 / 52 (1.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	Neuroprotect	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	0 / 52 (0.00%)	

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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30895296>