Clinical trial results:
Prehospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug administration In Cardiac arrest

Summary

EudraCT number	2014-000792-11
Trial protocol	GB
Global end of trial date	04 July 2019

Results information

Result version number	v1 (current)
This version publication date	18 July 2020
First version publication date	18 July 2020
Summary attachment (see zip file)	A Randomized Trial of Epinephrine in out-of-hospital cardiac arrest (A Randomized Trial of Epinephrine in out-of-hospital cardiac arrest.pdf)

Trial information

Trial identification

Sponsor protocol code	REGO-2014-612

Additional study identifiers

ISRCTN number	ISRCTN73485024
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Warwick
Sponsor organisation address	Gibbet Hill Raod, Coventry, United Kingdom,
Public contact	Prof Gavin Perkins, University of Warwick, 0044 02476550479, g.d.perkins@warwick.ac.uk
Scientific contact	Prof Gavin Perkins, University of Warwick, 0044 02476550479, g.d.perkins@warwick.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	27 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 October 2017
Global end of trial reached?	Yes
Global end of trial date	04 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the clinical effectiveness of adrenaline in the treatment of out of hospital cardiac arrest, measured as survival to 30 days.

Protection of trial subjects:

primary outcome-survival to 30 days. Adverse events and Serious adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 December 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Scientific research
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 8014
Worldwide total number of subjects	8014
EEA total number of subjects	8014

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)	23
Adults (18-64 years)	2656
From 65 to 84 years	3882
85 years and over	1453

Subject disposition

Recruitment

Recruitment details:

From December 2014 through October 2017, the multicenter, randomized, double-blind, placebo controlled PARAMEDIC2 trial was conducted by five National Health Service ambulance services in the United Kingdom.

Pre-assignment

Screening details:

Inclusion criteria: Out-of-hospital cardiac arrest; Advanced life support initiated and/or continued by ambulance service clinician.
Exclusion criteria: Known or apparent pregnancy or <16 years; Cardiac arrest caused by anaphylaxis or life threatening asthma; Adrenaline given prior to ambulance service clinician arrival; traumatic arrest (London)

Pre-assignment period milestones

Number of subjects started	10623[1]
Intermediate milestone: Number of subjects	Pack opened, before drug was given: 8103
Intermediate milestone: Number of subjects	Pack opened, drug was given: 8016
Number of subjects completed	8014

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Known or suspected to be <16 years of age: 268
Reason: Number of subjects	Known or suspected to be pregnant: 17
Reason: Number of subjects	Had return of spontaneous circulation: 615
Reason: Number of subjects	Had cardiac arrest secondary to anaphylaxis: 17
Reason: Number of subjects	Had CA secondary to life-threatening asthma: 183
Reason: Number of subjects	Received adrenaline before ambulance arrival: 1192
Reason: Number of subjects	Had traumatic arrest (London): 228
Reason: Number of subjects	Found to be pregnant after pack opened: 2
Reason: Number of subjects	Found to have ROSC after pack opened: 22
Reason: Number of subjects	Found do-not-resuscitate order after pack opened: 4
Reason: Number of subjects	Found to Have asthma after pack opened: 6
Reason: Number of subjects	Broken or contaminated syringes after pack opened: 4
Reason: Number of subjects	Found no intravenous access after pack opened: 2
Reason: Number of subjects	Had unknown reason after pack opened: 47
Reason: Number of subjects	Randomised but lost pack number (allocation info): 2

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: 10623 patients were assessed for eligibility. After excluding those ineligible patients, there were 8014 patients enrolled and given the trial drug.

Period 1

Period 1 title	Pre-hospital
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Unblinded data were only presented to the Data Monitoring Committee. The Trial Steering Committee were given blinded summary.

Arms

Are arms mutually exclusive?	Yes
Arm title	Adrenaline

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Experimental
Investigational medicinal product name	Adrenaline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm title	Placebo

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Number of subjects in period 1	Adrenaline	Placebo
Started	4015	3999
Completed	4015	3999

Period 2

Period 2 title	Hospital discharge
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Unblinded data were only presented to the Data Monitoring Committee. The Trial Steering Committee were given blinded summary.

Arms

Are arms mutually exclusive?	Yes
Arm title	Adrenaline

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Experimental
Investigational medicinal product name	Adrenaline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use, Intraosseous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm title	Placebo

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Number of subjects in period 2	Adrenaline	Placebo
Started	4015	3999
Completed	4015	3999

Period 3

Period 3 title	30 days post randomisation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Unblinded data were only presented to the Data Monitoring Committee. The Trial Steering Committee were given blinded summary.

Arms

Are arms mutually exclusive?	Yes
Arm title	Adrenaline

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Experimental
Investigational medicinal product name	Adrenaline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm title	Placebo

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Number of subjects in period 3	Adrenaline	Placebo
Started	4015	3999
Completed	4015	3999

Period 4

Period 4 title	3 months post randomisation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Unblinded data were only presented to the Data Monitoring Committee. The Trial Steering Committee were given blinded summary.

Arms

Are arms mutually exclusive?	Yes
Arm title	Adrenaline

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Experimental
Investigational medicinal product name	Adrenaline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm title	Placebo

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Number of subjects in period 4	Adrenaline	Placebo
Started	4015	3999
Completed	4015	3999

Period 5

Period 5 title	6 months post randomisation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Unblinded data were only presented to the Data Monitoring Committee. The Trial Steering Committee were given blinded summary.

Arms

Are arms mutually exclusive?	Yes
Arm title	Adrenaline

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Experimental
Investigational medicinal product name	Adrenaline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm title	Placebo

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Number of subjects in period 5	Adrenaline	Placebo
Started	4015	3999
Completed	4015	3999

Period 6

Period 6 title	12 months post randomisation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Unblinded data were only presented to the Data Monitoring Committee. The Trial Steering Committee were given blinded summary.

Arms

Are arms mutually exclusive?	Yes
Arm title	Adrenaline

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Experimental
Investigational medicinal product name	Adrenaline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm title	Placebo

Arm description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraosseous use, Intravenous use

Dosage and administration details:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of epinephrine (adrenaline) or 0.9% saline. Single doses of epinephrine or saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Number of subjects in period 6	Adrenaline	Placebo
Started	4015	3999
Completed	4015	3999

Baseline characteristics

Reporting groups	
Reporting group title	Adrenaline
Reporting group description:	
Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.	
Reporting group title	Placebo
Reporting group description:	
Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.	

Reporting group values	Adrenaline	Placebo	Total
Number of subjects	4015	3999	8014
Age categorical Units: Subjects			
Adolescents (12-17 years)	8	6	14
Adults (18-64 years)	1345	1311	2656
From 65-84 years	1923	1959	3882
85 years and over	735	718	1453
Missing	4	5	9
Age continuous Units: years			
arithmetic mean	69.7	69.8	
standard deviation	± 16.6	± 16.4	-
Gender categorical Units: Subjects			
Female	1406	1415	2821
Male	2609	2584	5193
Initial cardiac rhythm Units: Subjects			
Ventricular fibrillation	716	684	1400
Pulseless ventricular tachycardia	25	20	45
Asystole	2135	2194	4329
Pulseless electrical activity	955	937	1892
Bradycardia	20	16	36
Not otherwise identified with AED (Nonshockable)	39	34	73
Not otherwise identified with AED (Shockable)	29	44	73
Not identified	4	1	5
Missing	92	69	161
Cause of cardiac arrest Units: Subjects			
Medical cause	3656	3691	7347
Traumatic cause	66	57	123
Drowning	10	10	20
Drug overdose	74	72	146
Electrocution	0	1	1

Asphyxia	117	81	198
Not identified	1	2	3
Missing	91	85	176
Witness of cardiac arrest Units: Subjects			
None	1498	1505	3003
Paramedic	452	470	922
Bystander	2013	1967	3980
Not identified	1	1	2
Missing	51	56	107
CPR performed Units: Subjects			
By bystander	2382	2349	4731
By paramedic during witnessed event	452	471	923
Not identified	1	1	2
Missing	69	84	153
Not performed	1111	1094	2205
Return of spontaneous circulation Units: Subjects			
Yes	1457	468	1925
No	2518	3492	6010
Missing	40	39	79
Transportation of patient to hospital Units: Subjects			
Yes	2041	1227	3268
No	1974	2772	4746
Declaration of death by emergency department staff Units: Subjects			
Yes	988	689	1677
No	614	290	904
Not applicable because not transported	1974	2772	4746
Missing	439	248	687
Interval between emergency call and ambulance arrival at scene Units: minute			
median	6.7	6.6	
inter-quartile range (Q1-Q3)	4.3 to 9.7	4.2 to 9.6	-
Interval between emergency call and administration of trial agent Units: minute			
median	21.5	21.1	
inter-quartile range (Q1-Q3)	16.0 to 27.3	16.1 to 27.4	-
Interval between ambulance arrival at scene and departure Units: minute			
arithmetic mean	50.1	44.5	
standard deviation	± 21.8	± 18.3	-
Median interval between initiation of advanced life support and cessation Units: minute			
median	47.5	43.1	

inter-quartile range (Q1-Q3)	35.1 to 64.0	33.5 to 56.1	-

End points

End points reporting groups

Reporting group title	Adrenaline

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Placebo

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Adrenaline

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Placebo

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Adrenaline

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Placebo

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Adrenaline

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Placebo

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Adrenaline

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Placebo

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Adrenaline

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were

administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Placebo

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Primary: Survival at 30 days

End point title	Survival at 30 days

End point description:

End point type	Primary

End point timeframe:

30 days post randomisation

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4015	3999		
Units: Number of survivors				
Survived	130	94		
Deceased	3882	3901		

Statistical analyses

Statistical analysis title	Secondary analysis

Statistical analysis description:

Adjusted for patients' age, sex, interval between emergency call and ambulance arrival at scene, interval between ambulance arrival at scene and administration of the trial agent, initial cardiac rhythm, cause of cardiac arrest, whether the cardiac arrest was witnessed, and whether CPR was performed by a bystander.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8014
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.97

Statistical analysis title	Primary analysis
Statistical analysis description: Unadjusted analysis	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8014
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.82

Notes:

[1] - Unadjusted analysis.

Secondary: Survival event (sustained return of spontaneous circulation (ROSC))	
End point title	Survival event (sustained return of spontaneous circulation (ROSC))
End point description:	
End point type	Secondary
End point timeframe: Until admission and transfer of care to medical staff at the receiving hospital.	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4015	3999		
Units: Number of patients achieved ROSC				
Yes	947	319		
No	3026	3663		
Unknown	42	17		

Statistical analyses

Statistical analysis title	ROSC at hospital admission - unadjusted
Comparison groups	Placebo v Adrenaline

Number of subjects included in analysis	8014
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.14
upper limit	4.12

Statistical analysis title	ROSC at hospital admission - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8014
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	4.43

Secondary: Survival to hospital discharge

End point title	Survival to hospital discharge

End point description:

End point type	Secondary

End point timeframe:

The point at which the patient is discharged from the hospital acute care unit regardless of neurological status, outcome or destination.

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4015	3999		
Units: Number of patients survived				
Survived	128	91		
Deceased	3881	3904		

Unknown	6	4		

Statistical analyses

Statistical analysis title	Survival to hospital discharge - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8014
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.86

Statistical analysis title	Survival to hospital discharge - adjusted

Statistical analysis description:

Analysis was adjusted for patients' age, sex, interval between emergency call and ambulance arrival at scene, interval between ambulance arrival at scene and administration of the trial agent, initial cardiac rhythm, cause of cardiac arrest, whether the cardiac arrest was witnessed, and whether CPR was performed by a bystander.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8014
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	2

Secondary: Intensive care length of stay (survivors)

End point title	Intensive care length of stay (survivors)

End point description:

End point type	Secondary

End point timeframe:

From randomisation up to the first ICU discharge. Recurrent ICU admissions are not counted.

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146[2]	92[3]		
Units: Days				
median (inter-quartile range (Q1-Q3))	7.5 (3.0 to 15.0)	7.0 (3.5 to 12.5)		

Notes:

[2] - ICU survivors

[3] - ICU survivors

Statistical analyses

No statistical analyses for this end point

Secondary: Hospital length of stay (survivors)

End point title	Hospital length of stay (survivors)

End point description:

End point type	Secondary

End point timeframe:

From randomisation up to hospital discharge.

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	127	91		
Units: Days				
median (inter-quartile range (Q1-Q3))	21 (10 to 41)	20 (9 to 38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Hospital free survival in 30 days post randomisation

End point title	Hospital free survival in 30 days post randomisation

End point description:

Summary of days of free of hospital stay within the first 30 days survival or before death, whichever is sooner.

End point type	Secondary

End point timeframe:

30 days post randomisation.

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4007	3993		
Units: Days				
arithmetic mean (standard deviation)	0.3 (± 2.5)	0.2 (± 2.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: ICU free survival in 30 days post randomisation

End point title	ICU free survival in 30 days post randomisation

End point description:

Summary of days of free of ICU stay within the first 30 days survival or before death, whichever is sooner

End point type	Secondary

End point timeframe:

30 days post randomisation

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4006	3993		
Units: Days				
arithmetic mean (standard deviation)	0.8 (± 4.1)	0.5 (± 3.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Survival at 3 months

End point title	Survival at 3 months

End point description:

End point type	Secondary

End point timeframe:

3 months post randomisation

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4009	3991		
Units: Number of patients survived				
Survived	121	86		
Deceased	3888	3905		

Statistical analyses

Statistical analysis title	Survival at 3 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8000
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.87

Statistical analysis title	Survival at 3 months - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8000
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	2

Secondary: Survival at 6 months

End point title	Survival at 6 months

End point description:

End point type	Secondary

End point timeframe:
6 months post randomisation

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4006	3991		
Units: Number of patients survived				
Survived	117	85		
Deceased	3889	3906		

Statistical analyses

Statistical analysis title	Survival at 6 months - unadjusted
Comparison groups	Placebo v Adrenaline
Number of subjects included in analysis	7997
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.83

Statistical analysis title	Survival at 6 months - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7997
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.96

Secondary: Survival at 12 months

End point title	Survival at 12 months
End point description:	

End point type	Secondary
End point timeframe:	
12 months post randomisation	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4006	3991		
Units: Number of patients survived				
Survived	107	80		
Deceased	3899	3911		

Statistical analyses

Statistical analysis title	Survival at 12 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7997
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.8

Statistical analysis title	Survival at 12 months - adjusted
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	7997
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.92

Secondary: modified Rankin Scale at hospital discharge

End point title	modified Rankin Scale at hospital discharge

End point description:

mRS score is measured on a 7-point scale (from 0 (no symptom) to 6 (dead)). It is also summarised in binary category: Good (0-3) and Poor (4-6).

End point type	Secondary

End point timeframe:

At hospital discharge

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4007	3994		
Units: mRS score				
0 - No symptoms	12	15		
1 - No significant disability	17	10		
2 - Slight disability	23	29		
3 - Moderate disability	35	20		
4 - Moderately severe disability	12	8		
5 - Severe disability	27	8		
6 - Dead	3881	3904		

Attachments (see zip file)	mRS at hospital discharge/mRS at discharge.png

Statistical analyses

Statistical analysis title	mRS at discharge - unadjusted 0vs1-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.797
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.373
upper limit	1.704

Notes:

[4] - Results are listed separately. This record shows the odds of (0) vs odds of (1-6)

Statistical analysis title	mRS at discharge - unadjusted 0-1vs2-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Placebo v Adrenaline
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.157
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.677
upper limit	1.98

Notes:

[5] - Results are listed separately. This record shows the odds of (0-1) vs odds of (2-6)

Statistical analysis title	mRS at discharge - unadjusted 0-2vs3-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.959
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.654
upper limit	1.407

Notes:
[6] - Results are listed separately. This record shows the odds of (0-2) vs odds of (3-6)

Statistical analysis title	mRS at discharge - unadjusted 0-3vs4-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.176
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.608

Notes:
[7] - Results are listed separately. This record shows the odds of (0-3) vs odds of (4-6)

Statistical analysis title	mRS at discharge - unadjusted 0-4vs5-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.209
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.899
upper limit	1.625

Notes:
[8] - Results are listed separately. This record shows the odds of (0-4) vs odds of (5-6)

Statistical analysis title	mRS at discharge - unadjusted 0-5vs6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.408
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.071
upper limit	1.852

Notes:

[9] - Results are listed separately. This record shows the odds of (0-5) vs odds of (6)

Statistical analysis title	mRS at discharge - adjusted 0vs1-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.796
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.358
upper limit	1.769

Notes:

[10] - Results are listed separately. This record shows the odds of (0) vs odds of (1-6)

Statistical analysis title	mRS at discharge - adjusted 0-1vs2-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.156
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.658
upper limit	2.029

Notes:
[11] - Results are listed separately. This record shows the odds of (0-1) vs odds of (2-6)

Statistical analysis title	mRS at discharge - adjusted 0-2vs3-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Placebo v Adrenaline
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.651
upper limit	1.476

Notes:
[12] - Results are listed separately. This record shows the odds of (0-2) vs odds of (3-6)

Statistical analysis title	mRS at discharge - adjusted 0-3vs4-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.231
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.878
upper limit	1.727

Notes:
[13] - Results are listed separately. This record shows the odds of (0-3) vs odds of (4-6)

Statistical analysis title	mRS at discharge - adjusted 0-4vs5-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.263
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.914
upper limit	1.745

Notes:

[14] - Results are listed separately. This record shows the odds of (0-4) vs odds of (5-6)

Statistical analysis title	mRS at discharge - adjusted 0-5vs6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.508
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.115
upper limit	2.039

Notes:

[15] - Results are listed separately. This record shows the odds of (0-5) vs odds of (6)

Secondary: modified Rankin Scale at 3 months

End point title	modified Rankin Scale at 3 months

End point description:

mRS score is measured on a 7-point scale (from 0 (no symptom) to 6 (dead)). It is also summarised in binary category: Good (0-3) and Poor (4-6).

End point type	Secondary

End point timeframe:

at 3 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3986	3979		
Units: mRS score				
0 - No symptoms	20	20		
1 - No significant disability	30	20		
2 - Slight disability	10	11		
3 - Moderate disability	22	12		
4 - Moderately severe disability	6	5		
5 - Severe disability	10	6		
6 - Dead	3888	3905		

Statistical analyses

Statistical analysis title	mRS at 3 months - unadjusted
Comparison groups	Placebo v Adrenaline
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.328
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.979
upper limit	1.801

Statistical analysis title	mRS at 3 months - adjusted 0vs1-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.204
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.623
upper limit	2.325

Notes:
[16] - Results are listed separately. This record shows the odds of (0) vs odds of (1-6)

Statistical analysis title	mRS at 3 months - adjusted 0-1vs2-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.394
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.889
upper limit	2.184

Notes:
[17] - Results are listed separately. This record shows the odds of (0-1) vs odds of (2-6)

Statistical analysis title	mRS at 3 months - adjusted 0-2vs3-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.267
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.845
upper limit	1.9

Notes:
[18] - Results are listed separately. This record shows the odds of (0-2) vs odds of (3-6)

Statistical analysis title	mRS at 3 months - adjusted 0-3vs4-6
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.413

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.986
upper limit	2.025

Notes:

[19] - Results are listed separately. This record shows the odds of (0-3) vs odds of (4-6)

Statistical analysis title	mRS at 3 months - adjusted 0-4vs5-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.405
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.992
upper limit	1.99

Notes:

[20] - Results are listed separately. This record shows the odds of no symptom (0-4) vs odds of death (5-6)

Statistical analysis title	mRS at 3 months - adjusted 0-5vs6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.448
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.038
upper limit	2.02

Notes:

[21] - Results are listed separately. This record shows the odds of (0-5) vs odds of (6)

Secondary: modified Rankin Scale at 6 months

End point title	modified Rankin Scale at 6 months

End point description:

mRS score is measured on a 7-point scale (from 0 (no symptom) to 6 (dead)). It is also summarised in

binary category: Good (0-3) and Poor (4-6).

End point type	Secondary

End point timeframe:
at 6 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3990	3973		
Units: mRS score				
0 - No symptoms	25	19		
1 - No significant disability	22	13		
2 - Slight disability	10	9		
3 - Moderate disability	21	17		
4 - Moderately severe disability	7	2		
5 - Severe disability	16	7		
6 - Dead	3889	3906		

Statistical analyses

Statistical analysis title	mRS at 6 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	2.06

Statistical analysis title	mRS at 6 months - adjusted 0vs1-6

Statistical analysis description:
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	2.62

Notes:

[22] - Results are listed separately. This record shows the odds of (0) vs odds of (1-6)

Statistical analysis title	mRS at 6 months - adjusted 0-1vs2-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Placebo v Adrenaline
Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	2.65

Notes:

[23] - Results are listed separately. This record shows the odds of (0-1) vs odds of (2-6)

Statistical analysis title	mRS at 6 months - adjusted 0-2vs3-6

Statistical analysis description:

Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.

Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.26

Notes:
[24] - Results are listed separately. This record shows the odds of (0-2) vs odds of (3-6)

Statistical analysis title	mRS at 6 months - adjusted 0-3vs4-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	2.03

Notes:
[25] - Results are listed separately. This record shows the odds of (0-3) vs odds of (4-6)

Statistical analysis title	mRS at 6 months - adjusted 0-4vs5-6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	2.15

Notes:
[26] - Results are listed separately. This record shows the odds of (0-4) vs odds of (5-6)

Statistical analysis title	mRS at 6 months - adjusted 0-5vs6
Statistical analysis description:	
Partial proportional odds logistic regression. Ordinal proportional odds assumption violated.	
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	2.28

Notes:

[27] - Results are listed separately. This record shows the odds of (0-5) vs odds of (6)

Secondary: Favourable neurological outcome at hospital discharge

End point title	Favourable neurological outcome at hospital discharge

End point description:

mRS score is measured on a 7-point scale (from 0 (no symptom) to 6 (dead)). It is also summarised in binary category: Good (0-3) and Poor (4-6).

End point type	Secondary

End point timeframe:

at hospital discharge

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4007	3994		
Units: Numbers of patients with mRS 0-3				
Favourable	87	74		
Not favourable	3920	3920		

Statistical analyses

Statistical analysis title	Favourable neurological outcome - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.61

Statistical analysis title	Favourable neurological outcome - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	8001
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Mean difference (final values)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.68

Secondary: Favourable neurological outcome at 3 months

End point title	Favourable neurological outcome at 3 months
End point description:	
mRS score is measured on a 7-point scale (from 0 (no symptom) to 6 (dead)). It is also summarised in binary category: Good (0-3) and Poor (4-6).	
End point type	Secondary
End point timeframe:	
at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3986	3979		
Units: Number of patients with mRS 0-3				
Favourable	82	63		
Not favourable	3904	3916		

Statistical analyses

Statistical analysis title	Favourable neurological outcome 3m - unadjusted
Comparison groups	Placebo v Adrenaline

Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.82

Statistical analysis title	Favourable neurological outcome 3m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7965
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.01

Secondary: Favourable neurological outcome at 6 months

End point title	Favourable neurological outcome at 6 months

End point description:

mRS score is measured on a 7-point scale (from 0 (no symptom) to 6 (dead)). It is also summarised in binary category: Good (0-3) and Poor (4-6).

End point type	Secondary

End point timeframe:

at 6 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3990	3973		
Units: Number of patients with mRS 0-3				
Favourable	78	58		
Not favourable	3912	3915		

Statistical analyses

Statistical analysis title	Favourable neurological outcome 6m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.9

Statistical analysis title	Favourable neurological outcome 6m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	7963
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.97

Secondary: SF-12 Physical health at 3 months	
End point title	SF-12 Physical health at 3 months
End point description: As in the SF-12 manual: How to Score version 2 of the SF-12 Health Survey.	
End point type	Secondary
End point timeframe: at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	60		
Units: point				
arithmetic mean (standard deviation)	39.5 (± 12.6)	42.6 (± 11.6)		

Statistical analyses

Statistical analysis title	SF12 physical health at 3m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.25
upper limit	1.04

Statistical analysis title	SF12 physical health at 3m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.43
upper limit	2.36

Secondary: SF-12 Mental health at 3 months	
End point title	SF-12 Mental health at 3 months

End point description:

End point type	Secondary
End point timeframe: at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	60		
Units: point				
arithmetic mean (standard deviation)	48.8 (± 9.8)	50.0 (± 10.5)		

Statistical analyses

Statistical analysis title	SF12 mental health at 3m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.63
upper limit	2.28

Statistical analysis title	SF12 mental health at 3m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-1.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.32
upper limit	1.66

Secondary: SF-12 Physical health at 6 months	
End point title	SF-12 Physical health at 6 months
End point description:	
End point type	Secondary
End point timeframe:	
at 6 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	47		
Units: point				
arithmetic mean (standard deviation)	39.8 (± 12.6)	40.5 (± 11.9)		

Statistical analyses

Statistical analysis title	SF12 physical health at 6m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.24
upper limit	4

Statistical analysis title	SF12 physical health at 6m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.67
upper limit	3.28

Secondary: SF-12 Mental health at 6 months

End point title	SF-12 Mental health at 6 months
End point description:	

End point type	Secondary
End point timeframe:	
at 6 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	47		
Units: point				
arithmetic mean (standard deviation)	43.6 (± 13.0)	46.5 (± 13.1)		

Statistical analyses

Statistical analysis title	SF12 mental health at 6m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-2.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.76
upper limit	1.98

Statistical analysis title	SF12 mental health at 6m - adjusted
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-2.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	2.62

Secondary: EQ-5D-5L index score at 3 months

End point title	EQ-5D-5L index score at 3 months
End point description:	

End point type	Secondary
End point timeframe:	
at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	65		
Units: point				
arithmetic mean (standard deviation)	0.6 (± 0.4)	0.7 (± 0.3)		

Statistical analyses

Statistical analysis title	EQ-5D-5L index score at 3m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	0.04

Statistical analysis title	EQ-5D-5L index score at 3m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.06

Secondary: EQ-5D-5L VAS score at 3 months	
End point title	EQ-5D-5L VAS score at 3 months
End point description:	
End point type	Secondary
End point timeframe:	
at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	65		
Units: point				
arithmetic mean (standard deviation)	59.8 (± 25.1)	66.0 (± 24.8)		

Statistical analyses

Statistical analysis title	EQ-5D-5L VAS at 3m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-6.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.32
upper limit	1.83

Statistical analysis title	EQ-5D-5L VAS at 3m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-5.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.37
upper limit	3.22

Secondary: EQ-5D-5L VAS at 6 months

End point title	EQ-5D-5L VAS at 6 months
End point description:	

End point type	Secondary
End point timeframe:	
at 6 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	49		
Units: point				
arithmetic mean (standard deviation)	66.1 (± 26.0)	70.7 (± 26.0)		

Statistical analyses

Statistical analysis title	EQ-5D-5L VAS at 6m - unadjusted
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-4.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.96
upper limit	4.86

Statistical analysis title	EQ-5D-5L VAS at 6m - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-4.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.52
upper limit	5.23

Secondary: EQ-5D-5L index score at 6 months
End point title: EQ-5D-5L index score at 6 months
End point description:
End point type: Secondary
End point timeframe: at 6 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	49		
Units: point				
arithmetic mean (standard deviation)	0.6 (± 0.4)	0.7 (± 0.3)		

Statistical analyses

Statistical analysis title	EQ-5D-5L index score at 6m - unadjusted
Comparison groups	Placebo v Adrenaline
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.23
upper limit	0.05

Statistical analysis title	EQ-5D-5L index score at 6m - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.07

Secondary: Informant Questionnaire on Cognitive Decline in the Elderly at 3 months	
End point title	Informant Questionnaire on Cognitive Decline in the Elderly at 3 months
End point description:	

End point type	Secondary
End point timeframe:	
at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	55		
Units: point				
arithmetic mean (standard deviation)	3.3 (± 0.7)	3.4 (± 0.7)		

Statistical analyses

Statistical analysis title	IQCODE at 3 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.23

Statistical analysis title	IQCODE at 3 months - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.26

Secondary: Informant Questionnaire on Cognitive Decline in the Elderly at 6 months	
End point title	Informant Questionnaire on Cognitive Decline in the Elderly at

	6 months

End point description:

End point type	Secondary

End point timeframe:
at 6 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	48		
Units: point				
arithmetic mean (standard deviation)	3.1 (± 1.1)	3.2 (± 0.9)		

Statistical analyses

Statistical analysis title	IQCODE at 6 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.28

Statistical analysis title	IQCODE at 6 months - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.07

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.45
upper limit	0.31

Secondary: Two simple questions Q1 at 3 months

End point title	Two simple questions Q1 at 3 months

End point description:

End point type	Secondary

End point timeframe:
at 3 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	65		
Units: number of patients				
Yes	42	20		
No	47	45		

Statistical analyses

No statistical analyses for this end point

Secondary: Two simple questions Q1 at 6 months

End point title	Two simple questions Q1 at 6 months

End point description:
Question 1 at 6 months

End point type	Secondary

End point timeframe:
at 6 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	48		
Units: number of patients				
Yes	36	16		
No	42	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Mental Mini State Examination

End point title	Mental Mini State Examination
End point description:	
End point type	Secondary
End point timeframe:	
At 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	52		
Units: point				
arithmetic mean (standard deviation)	27.2 (± 3.4)	27.5 (± 3.1)		

Statistical analyses

Statistical analysis title	MMSE at 3 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.88

Statistical analysis title	MMSE at 3 months - adjusted
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.85
upper limit	0.81

Secondary: Hospital Anxiety and Depression scale - Anxiety score

End point title	Hospital Anxiety and Depression scale - Anxiety score
End point description:	

End point type	Secondary
End point timeframe:	
at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	62		
Units: point				
arithmetic mean (standard deviation)	6.4 (± 4.9)	5.3 (± 4.6)		

Statistical analyses

Statistical analysis title	HADS anxiety at 3 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	2.72

Statistical analysis title	HADS anxiety at 3 months - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	2.8

Secondary: Hospital Anxiety and Depression scale - Depression score	
End point title	Hospital Anxiety and Depression scale - Depression score
End point description:	
End point type	Secondary
End point timeframe:	
at 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	61		
Units: point				
arithmetic mean (standard deviation)	5.0 (± 4.3)	4.5 (± 4.4)		

Statistical analyses

Statistical analysis title	HADS depression at 3 months - unadjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.89
upper limit	2.02

Statistical analysis title	HADS depression at 3 months - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.05
upper limit	1.88

Secondary: Post Traumatic Stress Disorder (PTSD) civilian checklist	
End point title	Post Traumatic Stress Disorder (PTSD) civilian checklist
End point description:	

End point type	Secondary
End point timeframe:	
At 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	58		
Units: point				
arithmetic mean (standard deviation)	30.3 (± 13.1)	26.8 (± 12.3)		

Statistical analyses

Statistical analysis title	PCL-C at 3 months - unadjusted
Comparison groups	Adrenaline v Placebo

Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	7.81

Statistical analysis title	PCL-C at 3 months - adjusted
Comparison groups	Adrenaline v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	3.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	8.11

Secondary: Intensive care length of stay - deceased
End point title: Intensive care length of stay - deceased
End point description:
End point type: Secondary
End point timeframe: From ICU admission to death in ICU

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	414[28]	176[29]		
Units: day				
median (inter-quartile range (Q1-Q3))	2 (1 to 5)	3 (1 to 5)		

Notes:
[28] - Deceased in ICU
[29] - Deceased in ICU

Statistical analyses

No statistical analyses for this end point

Secondary: Hospital length of stay (deceased)

End point title	Hospital length of stay (deceased)

End point description:

End point type	Secondary

End point timeframe:
From randomisation to hospital death

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3881	3903		
Units: day				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Two simple questions Q1a at 3 months

End point title	Two simple questions Q1a at 3 months

End point description:
subquestion if Q1 is yes at 3 months

End point type	Secondary

End point timeframe:
3 months

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	20		
Units: number of patients				
Yes	35	17		
No	7	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Two simple questions Q2 at 3 months

End point title	Two simple questions Q2 at 3 months
End point description: Question 2 at 3 months	
End point type	Secondary
End point timeframe: 3 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	65		
Units: Number of patients				
Yes	34	32		
No	55	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Two simple questions Q1a at 6 months

End point title	Two simple questions Q1a at 6 months
End point description: Subqeustion if Q1 is yes at 6 months	
End point type	Secondary
End point timeframe: at 6 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	16		
Units: Number of patients				
Yes	30	10		
No	6	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Two simple questions Q2 at 6 months

End point title	Two simple questions Q2 at 6 months
End point description: Question 2 at 6 months	
End point type	Secondary
End point timeframe: at 6 months	

End point values	Adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	48		
Units: Number of patients				
Yes	35	25		
No	43	23		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

from randomisation up to hospital discharge

Adverse event reporting additional description:

An AE is: "Any untoward medical occurrence in a patient or clinical investigation participant taking part in health care research, which does not necessarily have a causal relationship with the research".

Assessment type	Systematic

Dictionary used

Dictionary name	Study protocol
Dictionary version	6.0

Reporting groups

Reporting group title	Adrenaline

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing 1 mg of epinephrine (adrenaline). Single doses of epinephrine were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Reporting group title	Placebo

Reporting group description:

Uniquely numbered but otherwise identical-appearing trial packs contained 10 prefilled syringes, with each syringe containing either 1 mg of 0.9% saline. Single doses of saline were administered by an intravenous or intraosseous route every 3 to 5 minutes.

Serious adverse events	Adrenaline	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4015 (0.00%)	0 / 3999 (0.00%)	
number of deaths (all causes)	3899	3911	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Adrenaline	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 4015 (0.02%)	1 / 3999 (0.03%)	
Cardiac disorders			
Patient fell	Additional description: Whilst moving the patient to the ambulance, the strecher wheel came off the garden path resulting in the trolley and patient falling into the garden. At the time of completing the form there is no evidence of injury or detrement to the patient.		
subjects affected / exposed	0 / 4015 (0.00%)	1 / 3999 (0.03%)	
occurrences (all)	0	1	
Equipment failure	Additional description: The paramedic was unable to clear the patient airway successfully due to equipment failure.		

subjects affected / exposed occurrences (all)	1 / 4015 (0.02%) 1	0 / 3999 (0.00%) 0	

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/30391366

http://www.ncbi.nlm.nih.gov/pubmed/30021076

http://www.ncbi.nlm.nih.gov/pubmed/31912202

http://www.ncbi.nlm.nih.gov/pubmed/31937351

http://www.ncbi.nlm.nih.gov/pubmed/27650864