Clinical trial results:
Vasculopathic Injury and Plasma as Endothelial Rescue in septic shock (SEPSIS) trial

Summary

EudraCT number	2016-000707-81
Trial protocol	DK
Global end of trial date	04 November 2016

Results information

Result version number	v1 (current)
This version publication date	06 May 2018
First version publication date	06 May 2018

Trial information

Trial identification

Sponsor protocol code	VIPER-SEPSIS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02875236
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Rigshospitalet, Section for Transfusion Medicine, Capitol Region Blood Bank
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, DK-2100
Public contact	Pär I. Johansson, Section for Transfusion Medicine, Capitol Region Blood Bank, 45 35452030, per.johansson@regionh.dk
Scientific contact	Pär I. Johansson, Section for Transfusion Medicine, Capitol Region Blood Bank, 45 35452030, per.johansson@regionh.dk

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	02 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2016
Global end of trial reached?	Yes
Global end of trial date	04 November 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Efficacy of octaplasLG® administration as compared to crystalloids (standard) in patients with septic shock

Protection of trial subjects:

Patients are closely monitored during the trial.
- Blood drawn only from already inserted catheter
- WBC must be between 4,000-12,000/mm3
- TRALI/TACO and anaphylaxis are closely monitored

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	2
From 65 to 84 years	2
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients are recruited from ITA at Bispebjerg Hospital in the period from 29/8-2016 to 26/9-2016

Pre-assignment

Screening details:

Patients admitted to the ICU were screened for inclusion in the trial

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Octaplas

Arm description: -

Arm type	Experimental
Investigational medicinal product name	OctaplasLG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Resuscitation fluid to patient with septic shock. No fixed dosage. OctaplasLG is given at 200 ml interval until patient reach adequate volume resuscitation

Arm title	Ringer-acetat

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Ringer-acetate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Resuscitation fluid to patient with septic shock. No fixed dosage. Ringer-acetate is given at 200 ml interval until patient reach adequate volume resuscitation

Number of subjects in period 1	Octaplas	Ringer-acetat
Started	2	3
Completed	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Octaplas
Reporting group description: -	
Reporting group title	Ringer-acetat
Reporting group description: -	

Reporting group values	Octaplas	Ringer-acetat	Total
Number of subjects	2	3	5
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)	0	2	2
From 65-84 years	1	1	2
85 years and over	1	0	1
Age continuous Units: years			
arithmetic mean	82	67	
full range (min-max)	78 to 85	60 to 73	-
Gender categorical Units: Subjects			
Female	2	1	3
Male	0	2	2

Subject analysis sets	
Subject analysis set title	Demographics
Subject analysis set type	Intention-to-treat
Subject analysis set description: Only five patients were included so the study was prematurely ended	

Reporting group values	Demographics		
Number of subjects	5		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	2		
From 65-84 years	2		
85 years and over	1		
Age continuous			
Units: years			
arithmetic mean	71		
full range (min-max)	60 to 85		
Gender categorical			
Units: Subjects			
Female	3		
Male	2		

End points

End points reporting groups

Reporting group title	Octaplas
Reporting group description: -	
Reporting group title	Ringer-acetat
Reporting group description: -	
Subject analysis set title	Demographics
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Only five patients were included so the study was prematurely ended	

Primary: Change in Microscan

End point title	Change in Microscan[1]
End point description:	
Change in microvascular perfusion using microscan	
End point type	Primary
End point timeframe:	
From baseline until 6h	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A this trial was premature ended with only 5 patients included an analysis of the primary endpoint were not performed

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: percentage				
number (not applicable)				

Notes:

[2] - Premature termination of the study therefore this analysis could not performed

[3] - Premature termination of the study therefore this analysis could not performed

Statistical analyses

No statistical analyses for this end point

Primary: Change in biomarkers

End point title	Change in biomarkers[4]
End point description:	
Change in biomarkers (sE-selectin, syndecan-1, thrombomodulin, sVE-cadherin, nucleosomes) indicative of endothelial activation and damage	
End point type	Primary
End point timeframe:	
From baseline to 6h	

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A this trial was premature ended with only 5 patients included an analysis of the primary endpoint were not performed

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: various				
number (not applicable)				

Notes:

[5] - Premature termination of the trial therefore this analysis was not performed

[6] - Premature termination of the trial therefore this analysis was not performed

Statistical analyses

No statistical analyses for this end point

Secondary: Mortality

End point title	Mortality

End point description:

Number of patients dying within 90 days

End point type	Secondary

End point timeframe:

Difference in 6h, 24h, 7, 30 and 90 days mortality

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Arbitary	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: SAE

End point title	SAE

End point description:

Number of SAE reported until day 30

End point type	Secondary

End point timeframe:

SAE reported until day 30

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: number	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Days in ventilator

End point title	Days in ventilator

End point description:

Mean value of the numbers of days the patients were on ventilation

End point type	Secondary

End point timeframe:

Days on ventilator until discharge or dead

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Number	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of stay in the ICU

End point title	Length of stay in the ICU

End point description:

Mean value of number of days the patients were admitted on the ICU

End point type	Secondary

End point timeframe:

From baseline until discharge from the ICU or dead

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: number	4	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Days on vasopressor

End point title	Days on vasopressor

End point description:

Mean value of number of days patients were on vasopressor treatment

End point type	Secondary

End point timeframe:

Number of days on vasopressor until discharge or death

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Number	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Bleeding requirement above 2 RBC / day

End point title	Bleeding requirement above 2 RBC / day

End point description:

Number of patients in each group with bleeding requirement above 2 RBC /day

End point type	Secondary

End point timeframe:

From baseline until 72h

End point values	Octaplas	Ringer-acetat		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	3		
Units: Number	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Baseline until day 30	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	OctaplasLG
Reporting group description: -	
Reporting group title	Ringer-Acetate
Reporting group description: -	

Serious adverse events	OctaplasLG	Ringer-Acetate	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	OctaplasLG	Ringer-Acetate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 3 (0.00%)	

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 adverse reaction were recorded during the study

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2016	Removal of statistical analysis NIRS. This removal did not impact patient safety or resulted in any ethical considerations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
02 November 2016	This trial was prematurely ended due to lack of patient. No safety concerns were observed during the trial	-

Notes:

Limitations and caveats

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

premature termination of the trial resulted in lack of patients included and therefore lack of statistical analysis

Notes: