Clinical trial results:
Vasculopathic Injury and Plasma as Endothelial Rescue – OCTAplas trial

Summary

EudraCT number	2014-000452-28
Trial protocol	DK
Global end of trial date	24 June 2016

Results information

Result version number	v1 (current)
This version publication date	21 January 2022
First version publication date	21 January 2022
Summary attachment (see zip file)	Article (Resuscitation of Endotheliopathy and Bleeding.pdf)

Trial information

Trial identification

Sponsor protocol code	VIPER-OCTA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02253082
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	31 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2016
Global end of trial reached?	Yes
Global end of trial date	24 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To conduct a pilot trial to assess the effects of OctaplasLG® on endothelial integrity, as compared to standard FFP, in a patient population experiencing severe endothelial dysfunction.

Protection of trial subjects:

As the patients are admitted to the hospital, standard of care is provided to the patients.
The excluding criteria prevent inclusion of patients not eligible for the trial.

Background therapy:

Standard of care

Evidence for comparator:

The comparator is FFP and i used as standard of care as coagulation factor replacement related to bleeding

Actual start date of recruitment	01 April 2014
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: 57
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	33
From 65 to 84 years	24

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From November 2014 to July 2016, 57 subjects (Intension-to-treat population) were randomized to obtain 44 evaluable patients.
Included patients were admitted to Rigshospitalet, Copenhagen University Hospital, Denmark, undergoing emergency surgery for thoracic aortic dissection

Pre-assignment

Screening details:

Patients were screened upon admission to the hospital

Pre-assignment period milestones

Number of subjects started	72[1]
Number of subjects completed	57

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 1
Reason: Number of subjects	Exclusion criteria meet: 10
Reason: Number of subjects	Intervention not available: 1
Reason: Number of subjects	Missed inclusion: 3

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: The number of 72 is the number of of patients screened. The number of 57 is the number of patients randomised and the number of 44 is the number of patients fulfilling per protocol and therefore the primary endpoint.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Data analyst[2]

Blinding implementation details:

research staff performed onsite randomization (1:1) by envelope opening. The randomization was done in a block size of 6; sequence and envelopes were generated and validated by 2 independent people otherwise not involved in the trial. Randomization was performed using Microsoft
Excel software (Microsoft, Redmond, WA)

Arms

Are arms mutually exclusive?	Yes
Arm title	OctaplasLG

Arm description:

Adminitration until bleeding control

Arm type	Experimental
Investigational medicinal product name	OctaplasLG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Administration until bleeding control

Arm title	Fresh frozen plasma (FFP)

Arm description:

Plasma adminitration until bleeding control.
This arm i standard of care.

Arm type	Active comparator
Investigational medicinal product name	FFP
Investigational medicinal product code	
Other name	Fresh frozen plasma
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Administration until bleeding control

Notes:

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: the laboratory staff performing the biomarkers analyses and the statistician were blinded to the allocation.

Number of subjects in period 1	OctaplasLG	Fresh frozen plasma (FFP)
Started	29	28
Completed	23	21
Not completed	6	7
Physician decision	1	1
Error in inclusion	1	-
dead before 24 hours	4	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	57	57	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adult (age 18 years or above)	57	57	
Gender categorical Units: Subjects			
Female	12	12	
Male	45	45	

End points

End points reporting groups

Reporting group title	OctaplasLG
Reporting group description:	
Adminitration until bleeding control	
Reporting group title	Fresh frozen plasma (FFP)
Reporting group description:	
Plasma adminitration until bleeding control. This arm i standard of care.	

Primary: Endothelial derived biomarkers

End point title	Endothelial derived biomarkers
End point description:	
The primary outcome measure was glycocalyx and endothelial injury as measured by plasma levels of endothelialderived biomarkers (syndecan-1, soluble thrombomodulin [sTM], soluble (s) E-selectin, sVE-cadherin) at24 hours after surgery compared to the baseline defined as 15 minutes before weaning from CPB	
End point type	Primary
End point timeframe:	
24 hours	

End point values	OctaplasLG	Fresh frozen plasma (FFP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	21		
Units: ng/ml				
median (inter-quartile range (Q1-Q3))				
Thrombomodulin	3.5 (1.8 to 6)	1.4 (0.3 to 4.1)		
Selectin	8.4 (2.3 to 21.4)	12.3 (-19.5 to 19.3)		
Cadherin	372.0 (221.1 to 522.1)	543.0 (223.6 to 686.3)		
Syndecan-1	-67.6 (-76.1 to -45.5)	-34.3 (-76.9 to -20.6)		

Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	Fresh frozen plasma (FFP) v OctaplasLG

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Mortality

End point title	Mortality

End point description:

End point type	Secondary

End point timeframe:

Mortality at day 30 and day 90

End point values	OctaplasLG	Fresh frozen plasma (FFP)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: number				
Day 30 mortality	6	7		

Statistical analyses

Statistical analysis title	Secondary endpoint
Comparison groups	OctaplasLG v Fresh frozen plasma (FFP)
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.76
Method	Fisher exact

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

For evaluation of safety, we followed severe adverse reactions, transfusion-associated ALI, and transfusion-associated cardiac overload in the first 30 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23

Reporting groups

Reporting group title	Octaplas

Reporting group description:

Intervention arm
Only SAE and SAR are recorded due to severly ill patients

Reporting group title	Standard FFP

Reporting group description:

The control arm.
Only SAE and SAR are recorded due to severly ill patients

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: As these patients are severly ill only SAEs and SARs are recorded

Serious adverse events	Octaplas	Standard FFP	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 29 (27.59%)	11 / 28 (39.29%)	
number of deaths (all causes)	6	7	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Ischaemia			
subjects affected / exposed	3 / 29 (10.34%)	4 / 28 (14.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction	Additional description: transfusion-associated circulatory overload (TACO)		
subjects affected / exposed	1 / 29 (3.45%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Transfusion	Additional description: Need for blood transfusion above 2 RBC within 24 hours		
subjects affected / exposed	4 / 29 (13.79%)	5 / 28 (17.86%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Anaphylactic shock			
subjects affected / exposed	0 / 29 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Octaplas	Standard FFP	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 28 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29863610