Clinical trial results:
An Open-label, Multicenter, Post-Marketing Requirement (PMR) Study to Investigate the Safety, Tolerability and Efficacy of Octaplas in the Management of Pediatric Patients Who Require Replacement of Multiple Coagulation Factors

Summary

EudraCT number	2018-004686-13
Trial protocol	Outside EU/EEA
Global end of trial date	04 December 2017

Results information

Result version number	v1 (current)
This version publication date	15 July 2020
First version publication date	15 July 2020

Trial information

Trial identification

Sponsor protocol code	LAS-212

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02050841
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Octapharma Pharmazeutika Produktionsges.m.b.H.
Sponsor organisation address	Oberlaaer Strasse 235, Vienna, Austria, 1100
Public contact	Clinical Research Department, Octapharma Pharmazeutika Produktionsges.m.b.H., franz-josef.tarmann@octapharma.com
Scientific contact	Clinical Research Department, Octapharma Pharmazeutika Produktionsges.m.b.H., franz-josef.tarmann@octapharma.com

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 July 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the safety and tolerability of Octaplas in the pediatric population by monitoring serious adverse events (SAEs), adverse drug reactions (ADRs), thrombotic events (TEs), thromboembolic events (TEEs) and hyperfibrinolytic events (HFEs), including laboratory parameters for metabolic derangements, renal function, and hematologic implications.

Protection of trial subjects:

This trial was conducted in accordance to the principles of ICH- GCP, ensuring that the rights, safety and well-being of patients are protected and in consistency with the Declaration of Helsinki.
Inclusion and exclusion criteria were carefully defined in order to protect subjects from contraindications, interactions with other medication and risk factors associated with the investigational medicinal product.
Throughout the study safety was assessed, such as of monitoring of ADRs, thrombotic events (TEs), thromboembolic events (TEEs), Hyperfibrinolytic event (HFEs) of causality and documentation of concomitant medication.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 July 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 50
Worldwide total number of subjects	50
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	5
Infants and toddlers (28 days-23	28

months)	
Children (2-11 years)	14
Adolescents (12-17 years)	3
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Paediatric patients who require replacement of multiple coagulation factors due to liver disease and/or cardiac surgery or liver transplantation.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Octaplas

Arm description:

Octaplas was used per the approved labeling for the product

Arm type	Experimental
Investigational medicinal product name	Octaplas
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Octaplas was used per the approved labeling for the product. The number of infusion episodes and volume of Octaplas administered within the 72-hour treatment period depended on the clinical setting. The infusion rate of Octaplas was not to exceed 0.020-0.025 mmol citrate per kg per minute. The minimum dose of the first infusion was 10 mL/kg or one unit unless a lower dose was medically justified.

Number of subjects in period 1	Octaplas
Started	50
Completed	49
Not completed	1
Use of prohibited medication	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	50	50	
Age categorical Units: Subjects			
Infants ≤2Years	37	37	
Children>2Years	13	13	
Age continuous Units: years			
arithmetic mean	2.0		
full range (min-max)	0 to 16	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	26	26	

End points

End points reporting groups

Reporting group title	Octaplas
Reporting group description:	
Octaplas was used per the approved labeling for the product	
Subject analysis set title	Safety population (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients who received at least one infusion of Octaplas	
Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients of the safety population with any measurements on the primary endpoint variables	
Subject analysis set title	Per-protocol population (PP)
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients who completed the infusion episode(s) and the final examination without major protocol deviations that may have had an impact on the evaluation of the study outcome parameters	
Subject analysis set title	Children >2 Years
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Children >2 Years	
Subject analysis set title	Infants ≤2 Years
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Infants ≤2 Years	
Subject analysis set title	EPL30-TEG
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Number of Participants With Clinically Significant Changes in Hemostatic Parameters as Measured by EPL30-TEG (estimated percent lysis)	
Subject analysis set title	ML30-ROTEM
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Number of Participants WithClinically Significant Changes in Hemostatic Parameters as Measured byThromboelastometry (ROTEM).	
Subject analysis set title	Octaplas - Pre-Infusion
Subject analysis set type	Full analysis
Subject analysis set description:	
Pre-Infusion Vital Signs	
Subject analysis set title	Octaplas - Post-Infusion
Subject analysis set type	Full analysis
Subject analysis set description:	
Post-Infusion Vital Signs	
Subject analysis set title	N (ratings)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Number of Patients	
Subject analysis set title	percentage (%)
Subject analysis set type	Safety analysis

Subject analysis set description:

Percentage

Subject analysis set title	CHANGE FROM PRE-INFUSION 1
Subject analysis set type	Full analysis

Subject analysis set description:

VITAL SIGNS DURING THE STUDY AND CHANGE FROM PRE-INFUSION TO POST-INFUSION

Primary: Number of Participants With Adverse Drug Reactions

End point title	Number of Participants With Adverse Drug Reactions[1]

End point description:

Number of Participants With Adverse Drug Reactions (e.g., Allergic Reactions, TEs, TEEs (Thromboembolic Events) and Hyperfibrinolytic Events)

End point type	Primary

End point timeframe:

up to 6 days

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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Safety population (SAF)			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: Number of patients				
Any SAE	5			
Any SAE related to Octaplas	0			
Any ADR	0			
Any ADR, SAE, HFE TEE, or TE leading to withdrawal	0			
Any ADR, SAE, HFE, TEE, or TE leading to death	1			
Any study death related to Octaplas	0			

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in White Blood Cells

End point title	Clinically Significant Changes in White Blood Cells[2]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: 10^3/µL				
median (full range (min-max))	5.3 (-4.7 to 28.3)	2.05 (-12.3 to 9.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Red Blood Cells

End point title	Clinically Significant Changes in Red Blood Cells[3]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[3] - 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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: 10^6/µL				
median (full range (min-max))	-0.34 (-1.4 to 0.6)	-0.06 (-1.8 to 1.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Hemoglobin

End point title	Clinically Significant Changes in Hemoglobin[4]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: g/dL				
median (full range (min-max))	-0.70 (-3.9 to 2.7)	0.8 (-4.6 to 5.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Hematocrit

End point title	Clinically Significant Changes in Hematocrit[5]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[5] - 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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: percentage				
median (full range (min-max))	-2.35 (-10.8 to 6.5)	1.35 (-14.6 to 16.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Mean Corpuscular Volume (MCV)

End point title	Clinically Significant Changes in Mean Corpuscular Volume (MCV)[6]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[6] - 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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: fL				
median (full range (min-max))	1.6 (-5.4 to 6.3)	1.85 (-22.8 to 9.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Mean Corpuscular Hemoglobin (MCH)

End point title	Clinically Significant Changes in Mean Corpuscular Hemoglobin (MCH)[7]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[7] - 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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: pg				
median (full range (min-max))	0.85 (-1.8 to 2.9)	1.00 (-8.3 to 5.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Mean Corpuscular Hemoglobin Concentration (MCHC)

End point title	Clinically Significant Changes in Mean Corpuscular Hemoglobin Concentration (MCHC)[8]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[8] - 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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: g/dL				
median (full range (min-max))	-0.15 (-0.9 to 4.2)	0.20 (-1.2 to 2.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Red Cell Distribution Width (RDW)

End point title	Clinically Significant Changes in Red Cell Distribution Width (RDW)[9]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[9] - 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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: percentage				
median (full range (min-max))	0.10 (-3.9 to 3.0)	0.40 (-2.1 to 4.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Clinically Significant Changes in Platelets

End point title	Clinically Significant Changes in Platelets[10]

End point description:

Assesses Pre- and Post-infusion for Infusion Episode 1

End point type	Primary

End point timeframe:

up to 6 days

Notes:

[10] - 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: Trial includes one arm only. For statistical analysis at least 2 arms are required, so no statistical analysis can be provided. Therefore, only results for this endpoint are provided

End point values	Children >2 Years	Infants ≤2 Years		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	37		
Units: 10^3/µL				
median (full range (min-max))	-105.5 (-210.0 to 15.0)	-167.00 (-410 to 215.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: International Normalized Ratio (INR)

End point title	Number of Participants With Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: International Normalized Ratio (INR)

End point description:

This hemostatic parameter is figured out in the lab and helps to diagnose a bleeding disorder or excessive clotting disorder. The change of INR before and after 1st Octaplas infusion was scrutinized by analyzing the shifts between the classifications given below.

End point type	Secondary

End point timeframe:

up to 6 days

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: Patients				
Shift from Not Clinically Significant to Normal	1			
Remained Normal	8			
Remained Not Clinically Significant	11			
Shift from Normal to Not Clinically Significant	25			
Shift to or from Clinically Significant	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: Prothrombin Time (PT)

End point title	Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: Prothrombin Time (PT)

End point description:

This hemostatic parameter is figured out in the lab and measures the time it takes for your blood to clot (the higher the PT the longer it takes your blood to clot). The change of PT before and after 1st Octaplas infusion was scrutinized by analyzing the shifts between the classifications given below.

End point type	Secondary

End point timeframe:

up to 6 days

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: Patients				
Shift from Not Clinically Significant to Normal	1			
Remained Normal	8			
Remained Not Clinically Significant	18			
Shift from Normal to Not Clinically Significant	19			
Shift to or from Clinically Significant	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: Thromboelastography (TEG) or Thromboelastometry (ROTEM).

End point title	Number of Participants With Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: Thromboelastography (TEG) or Thromboelastometry (ROTEM).

End point description:

TEG and ROTEM are methods of testing the efficiency of blood coagulation. The results were compared by looking at potential trends from TEG and ROTEM between pre-infusion vs post-infusion time points.

End point type	Secondary

End point timeframe:

up to 6 days

End point values	EPL30-TEG	ML30-ROTEM		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: Patients				
Shift from Not Clinically Significant to Normal	1	0		
Remained Normal	40	0		
Remained Not Clinically Significant	0	0		
Shift from Normal to Not Clinically Significant	0	0		
Shift to or from Clinically Significant	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: Activated Partial Thromboplastin Time (aPTT)

End point title	Number of Participants With Clinically Significant Changes in Hemostatic Parameters as Measured by the Following: Activated Partial Thromboplastin Time (aPTT)

End point description:

aPTT measures the length of time (in seconds) that it takes for clotting to occur in a test cube. The higher the number of seconds the longer it takes the blood to clot. The changes between pre - and post infusion were analyzed.

End point type	Secondary

End point timeframe:

up to 6 days

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: Patients				
Shift from Not Clinically Significant to Normal	5			
Remained Normal	18			
Remained Not Clinically Significant	12			
Shift from Normal to Not Clinically Significant	9			
Shift to or from Clinically Significant	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Volume (Dose in mL/kg) of Octaplas Used Per Infusion Episode for Each Patient.

End point title	Volume (Dose in mL/kg) of Octaplas Used Per Infusion Episode for Each Patient.

End point description:

Normal infusion: Replacement of multiple clotting factors Bypass priming: Limit hemodilution and reduce transfusion requirements Bypass warming up: Rewarm patients suffering from hypothermia during the surgery process

End point type	Secondary

End point timeframe:

up to 6 days

End point values	Safety population (SAF)			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: mL/kg				
arithmetic mean (standard deviation)				
Normal Infusion	15.0 (± 14.17)			
Bypass Priming	20.2 (± 7.82)			
Bypass Warming Up	15.9 (± 5.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Medically Significant Changes in Blood Pressure

End point title	Medically Significant Changes in Blood Pressure

End point description:

End point type	Secondary

End point timeframe:

up to 6 days

End point values	Octaplas - Pre-Infusion	Octaplas - Post-Infusion	CHANGE FROM PRE-INFUSION 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	50	50	50	
Units: mmHg				
arithmetic mean (standard deviation)				

Systolic Blood Pressure	75.66 (± 16.901)	79.96 (± 16.437)	4.30 (± 17.619)	
Diastolic Blood Pressure	46.28 (± 10.031)	50.00 (± 11.648)	3.72 (± 10.385)	

Statistical analyses

No statistical analyses for this end point

Secondary: Medically Significant Changes in Respiratory Rate

End point title	Medically Significant Changes in Respiratory Rate
End point description:	
End point type	Secondary
End point timeframe:	
up to 6 days	

End point values	Octaplas - Pre-Infusion	Octaplas - Post-Infusion	CHANGE FROM PRE-INFUSION 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	50	50	50	
Units: breaths/minute				
arithmetic mean (standard deviation)	21.17 (± 7.335)	23.79 (± 6.702)	1.17 (± 4.706)	

Statistical analyses

No statistical analyses for this end point

Secondary: Medically Significant Changes in Oxygen Saturation

End point title	Medically Significant Changes in Oxygen Saturation
End point description:	
End point type	Secondary
End point timeframe:	
up to 6 days	

End point values	Octaplas - Pre-Infusion	Octaplas - Post-Infusion	CHANGE FROM PRE-INFUSION 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	50	50	50	
Units: percentage in blood				
arithmetic mean (standard deviation)	96.86 (± 5.564)	98.33 (± 3.204)	1.50 (± 4.868)	

Statistical analyses

No statistical analyses for this end point

Secondary: Medically Significant Changes in Body Temperature

End point title	Medically Significant Changes in Body Temperature

End point description:

End point type	Secondary

End point timeframe:

up to 6 days

End point values	Octaplas - Pre-Infusion	Octaplas - Post-Infusion	CHANGE FROM PRE-INFUSION 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	50	50	50	
Units: Celsius				
arithmetic mean (standard deviation)	35.60 (± 2.023)	36.50 (± 1.597)	0.89 (± 1.425)	

Statistical analyses

No statistical analyses for this end point

Secondary: Medically Significant Changes in Heart Rate

End point title	Medically Significant Changes in Heart Rate

End point description:

End point type	Secondary

End point timeframe:

up to 6 days

End point values	Octaplas - Pre-Infusion	Octaplas - Post-Infusion	CHANGE FROM PRE-INFUSION 1	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	50	50	50	
Units: beats per minut				
arithmetic mean (standard deviation)	122.86 (± 30.528)	132.80 (± 26.439)	9.94 (± 26.282)	

Statistical analyses

No statistical analyses for this end point

Secondary: Count of Investigator's Assessment of Overall Safety Observed for Patients by Category

End point title	Count of Investigator's Assessment of Overall Safety Observed for Patients by Category

End point description:

Categories: (Assessed to Have Overall Safety of 'Excellent', Assessed to Have Overall Safety of 'Moderate', Assessed to Have Overall Safety of 'Poor')

End point type	Secondary

End point timeframe:

up to 6 days

End point values	N (ratings)	percentage (%)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	50	50		
Units: Patients				
Excellent	50	100		
Moderate	0	0		
Poor	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Throughout the whole 72-hour study treatment period until final examination 72 hours after end of last study infusion episode

Adverse event reporting additional description:

Unrelated, non-serious AEs observed during the study were not captured in the eCRF. Only ADRs, TEs, TEEs, and HFEs were to be recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Octaplas

Reporting group description:

Octaplas was used per the approved labeling for the product

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: Only ADRs were to be reported. Unrelated, non-serious AEs observed during the study were not captured . No ADRs were reported during the study .

Serious adverse events	Octaplas		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 50 (10.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Iatrogenic injury			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hypotension			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Haemorrhage coronary artery			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracardiac thrombus			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Portal vein thrombosis			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Octaplas		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2015	Amendment #4 was issued to primarily update conditions for storage and use, since new stability data had been approved by FDA.
18 March 2015	Amendment #3 was issued to primarily apply several enhancements.
03 February 2016	Amendment #5 was issued to primarily apply several enhancements.
09 September 2016	Amendment#7: - Use of Octaplas to Prime Cardiopulmonary Bypass (CPB):Language was added into the protocol in order to explain that patients who undergo cardiac surgery and receive Octaplas solely for the priming of the CPB circuit are qualified for enrollment and will be part of the full analysis set - Reduction of Age Categories -The end of study timeline has been revised
19 November 2016	Amendment#8: The timing of the pre-and post-infusion samples for patients on cardiopulmonary-bypass was clarified in the protocol.
29 November 2017	Amendment#9: Given that there have been no safety concerns thus far in all age groups and since most patients meeting the eligibility criteria have the required surgery at an early stage in their life, i.e. 0-2 years, the planned enrollment for the 2-16 year age category was changed from a minimum of 17 patients to a minimum of 13 patients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported