Clinical trial results:
An open-label, multicenter, Post-Marketing Requirement study to investigate the safety and tolerability of octaplas™ in the management of pediatric patients who require therapeutic plasma exchange.

Summary

EudraCT number	2020-000650-10
Trial protocol	Outside EU/EEA
Global end of trial date	27 January 2019

Results information

Result version number	v1 (current)
This version publication date	12 March 2020
First version publication date	12 March 2020

Trial information

Trial identification

Sponsor protocol code	LAS-213

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01938378
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Octapharma
Sponsor organisation address	121 River Street, Hoboken, United States, 07030
Public contact	Michael Eppolito, Octapharma, michael.eppolito@octapharma.com
Scientific contact	Michael Eppolito, Octapharma, michael.eppolito@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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 January 2019
Global end of trial reached?	Yes
Global end of trial date	27 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the safety and tolerability of octaplas™ in the pediatric patients undergoing therapeutic plasma exchange (TPE) by monitoring ADRs, TEs, TEEs, and by measuring safety laboratory parameters.

Protection of trial subjects:

This trial was conducted in accordance to the principles of 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 occurrence of SAEs, ADRs, TEs, TEEs, and safety labs.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 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: 41
Worldwide total number of subjects	41
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)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	15
Adolescents (12-17 years)	17
Adults (18-64 years)	9
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male or female patients aged 2 years through 20 years of age requiring therapeutic plasma exchange.

Period 1

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

Arms

Arm title	Octaplas

Arm description:

Therapeutic plasma exchange with Octaplas

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

Dosage and administration details:

The recommended dose is a total plasma volume between 40 to 60 mL/kg, as prescribed by the treating physician.

Number of subjects in period 1	Octaplas
Started	41
Completed	41

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial (Overall Period)
Reporting group description: -	

Reporting group values	Overall Trial (Overall Period)	Total	
Number of subjects	41	41	
Age categorical Units: Subjects			
Age Group 1 (2- <12)	15	15	
Age Group 2 (12- <17)	13	13	
Age Group 3 (≥17)	13	13	
Age continuous			
Continuous age in years			
Units: years			
arithmetic mean	12.3		
standard deviation	± 5.40	-	
Gender categorical			
Gender of patients			
Units: Subjects			
Female	23	23	
Male	18	18	
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	39	39	
Unknown or Not Reported	1	1	
Race Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	7	7	
White	32	32	
More than one race	0	0	
Unknown or Not Reported	0	0	

Subject analysis sets	
Subject analysis set title	Age Group 1 (2-<12)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Ages 2 to <12	
Subject analysis set title	Age Group 2 (12-<17)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Ages 12 to <17	

Subject analysis set title	Age Group 3 (≥17)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Ages ≥17

Reporting group values	Age Group 1 (2- <12)	Age Group 2 (12- <17)	Age Group 3 (≥17)
Number of subjects	15	13	13
Age categorical Units: Subjects			
Age Group 1 (2- <12)	15	0	0
Age Group 2 (12- <17)	0	13	0
Age Group 3 (≥17)	0	0	13
Age continuous			
Continuous age in years			
Units: years			
arithmetic mean	6.1	13.8	18.1
standard deviation	± 2.34	± 1.52	± 1.04
Gender categorical			
Gender of patients			
Units: Subjects			
Female	12	7	4
Male	3	6	9
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	15	12	12
Unknown or Not Reported	0	1	0
Race Units: Subjects			
American Indian or Alaska Native	0	2	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	2	3
White	13	9	10
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Octaplas
Reporting group description: Therapeutic plasma exchange with Octaplas	
Subject analysis set title	Age Group 1 (2-<12)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Ages 2 to <12	
Subject analysis set title	Age Group 2 (12-<17)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Ages 12 to <17	
Subject analysis set title	Age Group 3 (≥17)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Ages ≥17	

Primary: Monitoring of Adverse Drug Reactions Caused by the Octaplas™Used for Plasma Exchange.

End point title	Monitoring of Adverse Drug Reactions Caused by the Octaplas™Used for Plasma Exchange.[1]
End point description:	
End point type	Primary
End point timeframe: up to 8 days including the 24 hour follow-up from treatment	

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: Count of Adverse Drug Reactions

End point values	Octaplas	Age Group 1 (2-<12)	Age Group 2 (12-<17)	Age Group 3 (≥17)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	15	13	13
Units: events	8	0	5	3

Statistical analyses

No statistical analyses for this end point

Primary: Monitoring of TEs and TEEs Caused by the Octaplas™Used for Plasma Exchange.

End point title	Monitoring of TEs and TEEs Caused by the Octaplas™Used for Plasma Exchange.[2]
End point description:	

End point type	Primary

End point timeframe:

up to 8 days including the 24 hour follow-up from treatment

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: Count of TEs and TEEs

End point values	Octaplas	Age Group 1 (2-<12)	Age Group 2 (12-<17)	Age Group 3 (≥17)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	15	13	13
Units: event	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Blood Urea Nitrogen Levels from Pre-TPE to Post-TPE

End point title	Assessment of Blood Urea Nitrogen Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[3]			
Units: mg/dL				
arithmetic mean (standard deviation)				
TPE 1	-1.4 (± 6.56)			
TPE 2	1.2 (± 4.69)			
TPE 3	1.1 (± 3.21)			
TPE 4	1.5 (± 2.67)			
TPE 5	-0.5 (± 4.36)			
TPE 6	-1.0 (± 0)			

Notes:

[3] - TPE 1 34 subj.
TPE 2 17 subj.
TPE 3 11 subj.
TPE 4 8 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Carbon Dioxide Levels from Pre-TPE to Post-TPE

End point title	Assessment of Carbon Dioxide Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[4]			
Units: mmol/L				
arithmetic mean (standard deviation)				
TPE 1	2.2 (± 3.03)			
TPE 2	0.5 (± 2.79)			
TPE 3	1.2 (± 1.72)			
TPE 4	1.0 (± 2.98)			
TPE 5	0.3 (± 5.50)			
TPE 6	3.0 (± 0)			

Notes:

[4] - TPE 1 34 subj.
TPE 2 17 subj.
TPE 3 11 subj.
TPE 4 8 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Chloride Levels from Pre-TPE to Post-TPE

End point title	Assessment of Chloride Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[5]			
Units: mmol/L				
arithmetic mean (standard deviation)				
TPE 1	0.5 (± 3.31)			
TPE 2	0.6 (± 2.72)			
TPE 3	-0.3 (± 2.37)			
TPE 4	-0.9 (± 2.59)			
TPE 5	1.0 (± 6.78)			
TPE 6	-3.0 (± 0)			

Notes:

[5] - TPE 1 34 subj.
TPE 2 17 subj.
TPE 3 11 subj.
TPE 4 8 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Creatinine Levels from Pre-TPE to Post-TPE

End point title	Assessment of Creatinine Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[6]			
Units: mg/dl				
arithmetic mean (standard deviation)				
TPE 1	-0.4 (± 1.10)			
TPE 2	-0.1 (± 0.31)			
TPE 3	-0.1 (± 0.22)			
TPE 4	0.0 (± 0.09)			
TPE 5	0.1 (± 0.09)			
TPE 6	0.0 (± 0.0)			

Notes:

[6] - TPE 1 34 subj.
TPE 2 17 subj.
TPE 3 11 subj.
TPE 4 8 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Glucose Levels from Pre-TPE to Post-TPE

End point title	Assessment of Glucose Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[7]			
Units: mg/dl				
arithmetic mean (standard deviation)				
TPE 1	-12.0 (± 65.83)			
TPE 2	12.5 (± 44.76)			
TPE 3	22.6 (± 45.69)			
TPE 4	-44.3 (± 158.61)			
TPE 5	15.8 (± 38.59)			
TPE 6	-2.0 (± 0)			

Notes:

[7] - TPE 1 34 subj.
TPE 2 17 subj.
TPE 3 11 subj.
TPE 4 8 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Potassium Levels from Pre-TPE to Post-TPE

End point title	Assessment of Potassium Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[8]			
Units: mmol/L				
arithmetic mean (standard deviation)				
TPE 1	-0.1 (± 0.54)			
TPE 2	0.1 (± 0.26)			
TPE 3	0.1 (± 0.49)			
TPE 4	-0.2 (± 0.65)			
TPE 5	-0.1 (± 0.61)			
TPE 6	-0.7 (± 0)			

Notes:

[8] - TPE 1 34 subj.
TPE 2 17 subj.
TPE 3 11 subj.
TPE 4 8 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Sodium Levels from Pre-TPE to Post-TPE

End point title	Assessment of Sodium Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[9]			
Units: mmol/L				
arithmetic mean (standard deviation)				
TPE 1	1.6 (± 2.41)			
TPE 2	1.5 (± 1.84)			
TPE 3	1.5 (± 2.84)			
TPE 4	0.8 (± 1.75)			
TPE 5	1.0 (± 2.16)			
TPE 6	2.0 (± 0)			

Notes:

[9] - TPE 1 34 subj.
TPE 2 17 subj.
TPE 3 11 subj.
TPE 4 8 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Leukocyte Levels from Pre-TPE to Post-TPE

End point title	Assessment of Leukocyte Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[10]			
Units: 10^9/L				
arithmetic mean (standard deviation)				
TPE 1	0.9 (± 3.80)			
TPE 2	1.2 (± 3.93)			
TPE 3	-0.5 (± 2.44)			
TPE 4	1.2 (± 1.14)			
TPE 5	1.6 (± 1.55)			
TPE 6	3.3 (± 0)			

Notes:

[10] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Erythrocyte Levels from Pre-TPE to Post-TPE

End point title	Assessment of Erythrocyte Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[11]			
Units: 10^12/L				
arithmetic mean (standard deviation)				
TPE 1	0.1 (± 0.26)			
TPE 2	0.1 (± 0.27)			
TPE 3	0.1 (± 0.26)			
TPE 4	0.1 (± 0.17)			
TPE 5	-0.1 (± 0.49)			
TPE 6	-0.1 (± 0)			

Notes:

[11] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Hemoglobin Levels from Pre-TPE to Post-TPE

End point title	Assessment of Hemoglobin Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[12]			
Units: g/dL				
arithmetic mean (standard deviation)				
TPE 1	0.4 (± 0.74)			
TPE 2	0.3 (± 0.74)			
TPE 3	0.3 (± 0.70)			
TPE 4	-0.1 (± 0.67)			
TPE 5	-0.5 (± 1.44)			
TPE 6	-0.4 (± 0)			

Notes:

[12] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Hematocrit Levels from Pre-TPE to Post-TPE

End point title	Assessment of Hematocrit Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[13]			
Units: % of the blood that is red blood cells				
arithmetic mean (standard deviation)				
TPE 1	1.1 (± 2.12)			
TPE 2	0.8 (± 2.39)			
TPE 3	1.0 (± 2.37)			
TPE 4	0.6 (± 1.25)			
TPE 5	-1.2 (± 4.03)			
TPE 6	-1.6 (± 0)			

Notes:

[13] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Mean Corpuscular Volume Levels from Pre-TPE to Post-TPE

End point title	Assessment of Mean Corpuscular Volume Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[14]			
Units: fL				
arithmetic mean (standard deviation)				
TPE 1	0.2 (± 1.21)			
TPE 2	0.3 (± 1.55)			
TPE 3	-0.1 (± 1.55)			
TPE 4	-0.3 (± 2.01)			
TPE 5	-0.1 (± 2.13)			
TPE 6	-2.0 (± 0)			

Notes:

[14] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Mean Corpuscular Hemoglobin Levels from Pre-TPE to Post-TPE

End point title	Assessment of Mean Corpuscular Hemoglobin Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[15]			
Units: pg				
arithmetic mean (standard deviation)				
TPE 1	0.1 (± 0.70)			
TPE 2	0.1 (± 0.77)			
TPE 3	-0.2 (± 0.58)			
TPE 4	-0.8 (± 1.18)			
TPE 5	-0.4 (± 0.31)			
TPE 6	-0.2 (± 0)			

Notes:

[15] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.

TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Mean Corpuscular Hemoglobin Concentration Levels from Pre-TPE to Post-TPE

End point title	Assessment of Mean Corpuscular Hemoglobin Concentration Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[16]			
Units: g/dL				
arithmetic mean (standard deviation)				
TPE 1	0.1 (± 0.75)			
TPE 2	0 (± 0.97)			
TPE 3	-0.2 (± 0.91)			
TPE 4	-0.8 (± 1.15)			
TPE 5	-0.5 (± 0.62)			
TPE 6	0.4 (± 0)			

Notes:

[16] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Mean Red Cell Distribution Width Levels from Pre-TPE to Post-TPE

End point title	Assessment of Mean Red Cell Distribution Width Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in

number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[17]			
Units: % red blood cell variation volume/size				
arithmetic mean (standard deviation)				
TPE 1	0.0 (± 0.26)			
TPE 2	0.1 (± 0.37)			
TPE 3	-0.1 (± 0.33)			
TPE 4	0.0 (± 0.25)			
TPE 5	0.3 (± 0.52)			
TPE 6	-0.2 (± 0)			

Notes:

[17] - TPE 1 34 subj.
TPE 2 18 subj.
TPE 3 9 subj.
TPE 4 7 subj.
TPE 5 4 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Assessment of Mean Ionized Calcium Levels from Pre-TPE to Post-TPE

End point title	Assessment of Mean Ionized Calcium Levels from Pre-TPE to Post-TPE

End point description:

Blood samples compare levels before each TPE (therapeutic plasma exchange) and after each TPE. Pre-TPE is within 24 hours before TPE start; Post-TPE is 30 minutes to 3 hours after TPE end. Differences in number of subjects analyzed for each TPE due to not all patients receiving multiple blood draws/TPEs.

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[18]			
Units: mmol/L				
arithmetic mean (standard deviation)				
TPE 1	-0.030 (± 0.0927)			
TPE 2	0.026 (± 0.1203)			

TPE 3	1.026 (± 0.0684)			
TPE 4	0.011 (± 0.0995)			
TPE 5	-0.032 (± 0.1089)			
TPE 6	-0.075 (± 0)			

Notes:

[18] - TPE 1 28 subj.
TPE 2 14 subj.
TPE 3 12 subj.
TPE 4 8 subj.
TPE 5 6 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator's Assessment of Overall Safety

End point title	Investigator's Assessment of Overall Safety

End point description:

Excellent: defined as the treatment was well tolerated by the patient; Moderate: defined as ADR(s) were observed, but easily resolved or not clinically significant; Poor: defined as ADR(s) were observed requiring significant medical intervention

End point type	Secondary

End point timeframe:

up to 8 days including the 24 hour follow-up

End point values	Octaplas			
Subject group type	Reporting group			
Number of subjects analysed	41[19]			
Units: participants				
Patients Who Underwent TPE 1 - Excellent	37			
Patients Who Underwent TPE 1 - Moderate	4			
Patients Who Underwent TPE 1 - Poor	0			
Patients Who Underwent TPE 2 - Excellent	25			
Patients Who Underwent TPE 2 - Moderate	1			
Patients Who Underwent TPE 2 - Poor	0			
Patients Who Underwent TPE 3 - Excellent	18			
Patients Who Underwent TPE 3 - Moderate	0			
Patients Who Underwent TPE 3 - Poor	0			
Patients Who Underwent TPE 4 - Excellent	9			
Patients Who Underwent TPE 4 - Moderate	1			
Patients Who Underwent TPE 4 - Poor	0			
Patients Who Underwent TPE 5 - Excellent	6			

Patients Who Underwent TPE 5 - Moderate	0			
Patients Who Underwent TPE 5 - Poor	0			
Patients Who Underwent TPE 6 - Excellent	1			
Patients Who Underwent TPE 6 - Moderate	0			
Patients Who Underwent TPE 6 - Poor	0			

Notes:

[19] - TPE 1 41 subj.
TPE 2 26 subj.
TPE 3 18 subj.
TPE 4 10 subj.
TPE 5 6 subj.
TPE 6 1 subj.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 8 Days

Adverse event reporting additional description:

ADRs will be elicited using a standard non-leading question such as "How have you been since the last evaluation?" If children or adolescent patients are unable to adequately understand and respond to this question, the information will be obtained from the patient's guardian and/or Investigator or study nurse.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Octaplas

Reporting group description:

Therapeutic plasma exchange with Octaplas

Reporting group title	Pediatric Patients Undergoing TPE Age Group 1

Reporting group description:

Age Group 1
(2-<12)

Reporting group title	Pediatric Patients Undergoing TPE Age Group 2

Reporting group description:

Age Group 2
(12-<17)

Reporting group title	Pediatric Patients Undergoing TPE Age Group 3

Reporting group description:

Age Group 3
(≥17)

Serious adverse events	Octaplas	Pediatric Patients Undergoing TPE Age Group 1	Pediatric Patients Undergoing TPE Age Group 2
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 41 (2.44%)	1 / 15 (6.67%)	0 / 13 (0.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	1	1	0
General disorders and administration site conditions			
Multi-organ Failure			
subjects affected / exposed	1 / 41 (2.44%)	1 / 15 (6.67%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0

Serious adverse events	Pediatric Patients Undergoing TPE Age		

	Group 3		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Multi-organ Failure			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Octaplas	Pediatric Patients Undergoing TPE Age Group 1	Pediatric Patients Undergoing TPE Age Group 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 41 (9.76%)	0 / 15 (0.00%)	3 / 13 (23.08%)
Investigations			
Inflammatory marker increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Citrate toxicity			
subjects affected / exposed	2 / 41 (4.88%)	0 / 15 (0.00%)	2 / 13 (15.38%)
occurrences (all)	2	0	2
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 41 (2.44%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	1 / 41 (2.44%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 15 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 15 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Pediatric Patients Undergoing TPE Age Group 3		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)		
Investigations			
Inflammatory marker increased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Citrate toxicity			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Urticaria subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		

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