Clinical trial results:
A Phase III, randomized, double-blind, multicenter study to assess the efficacy and safety of OCTAPLEX, a four-factor prothrombin complex concentrate (4F-PCC), compared to the 4F-PCC Beriplex® P/N (Kcentra), for the reversal of vitamin K antagonist induced anticoagulation in patients needing urgent surgery with significant bleeding risk.

Summary

EudraCT number	2016-002649-41
Trial protocol	DE PL ES BG RO
Global end of trial date	08 November 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	LEX-209

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02740335
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Octapharma Pharmazeutika Produktionsges.m.b.H
Sponsor organisation address	Oberlaaerstr. 235, Vienna, Austria, 1100
Public contact	Clinical Research & Development, Octapharma Pharmazeutika Produktionsges.m.b.H, +43 (1) 610 320 , dmitrii.matveev@octapharma.com
Scientific contact	Clinical Research & Development, Octapharma Pharmazeutika Produktionsges.m.b.H, +43 (1) 610 320 , dmitrii.matveev@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	08 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 November 2021
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 demonstrate that the efficacy of OCTAPLEX as a reversal agent in patients under VKA therapy with the need for urgent surgery with significant bleeding risk is clinically non-inferior to Beriplex® P/N (Kcentra).

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, national regulatory requirements and FDA Code of Federal Regulations.
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 monitoring of AEs, SAEs, concomitant medication and vital status.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 June 2017
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	Romania: 51
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Georgia: 43
Country: Number of subjects enrolled	Belarus: 7
Country: Number of subjects enrolled	Ukraine: 94
Worldwide total number of subjects	208
EEA total number of subjects	51

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)	78
From 65 to 84 years	121
85 years and over	9

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with reversal of anticoagulation due to vitamin K antagonists needing urgent surgery associated with significant bleeding risk were screened according to predefined in- and exclusion criteria.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

IP was assigned using IRT and prepared for infusion by unblinded site personnel. Investigational product was prepared and infused in a manner that blinded the investigator and other blinded site personnel to the study treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Octaplex

Arm description:

Patients received 1 Octaplex infusion intravenously

Arm type	Experimental
Investigational medicinal product name	Octaplex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Investigational product was administered by IV infusion at a rate of 0.12 mL/kg/min (~3 units/kg/min), up to a maximum rate of 8.4 mL/min (~210 units/min). The total volume of IP used and time of infusion was recorded. Infusion lines were to be flushed with 0.9% sodium chloride. One single infusion of IP was administered per patient

Arm title	Kcentra

Arm description:

Patients received 1 Beriplex® P/N (Kcentra) infusion intravenously.

Arm type	Experimental
Investigational medicinal product name	Beriplex® P/N [Kcentra],
Investigational medicinal product code	
Other name	Kcentra
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Investigational product was administered by IV infusion at a rate of 0.12 mL/kg/min (~3 units/kg/min), up to a maximum rate of 8.4 mL/min (~210 units/min). The total volume of IP used and time of infusion was recorded. Infusion lines were to be flushed with 0.9% sodium chloride. One single infusion of IP was administered per patient

Number of subjects in period 1	Octaplex	Kcentra
Started	105	103
Completed	105	103

Baseline characteristics

Reporting groups	
Reporting group title	Octaplex
Reporting group description:	
Patients received 1 Octaplex infusion intravenously	
Reporting group title	Kcentra
Reporting group description:	
Patients received 1 Beriplex® P/N (Kcentra) infusion intravenously.	

Reporting group values	Octaplex	Kcentra	Total
Number of subjects	105	103	208
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean full range (min-max)	 65.6 31 to 90	 66.8 32 to 92	 -
Gender categorical Units: Subjects			
Female	47	43	90
Male	58	60	118

Subject analysis sets	
Subject analysis set title	Randomized Population (RAND)
Subject analysis set type	Full analysis
Subject analysis set description:	
The RAND population includes all randomized patients irrespective of whether they received treatment.	
Subject analysis set title	Safety Analysis Population (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The SAF population includes all randomized patients who received IP.	

Reporting group values	Randomized Population (RAND)	Safety Analysis Population (SAF)	
Number of subjects	208	208	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean full range (min-max)	 66.2 31 to 92		
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Octaplex
Reporting group description:	
Patients received 1 Octaplex infusion intravenously	
Reporting group title	Kcentra
Reporting group description:	
Patients received 1 Beriplex® P/N (Kcentra) infusion intravenously.	
Subject analysis set title	Randomized Population (RAND)
Subject analysis set type	Full analysis
Subject analysis set description:	
The RAND population includes all randomized patients irrespective of whether they received treatment.	
Subject analysis set title	Safety Analysis Population (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The SAF population includes all randomized patients who received IP.	

Primary: Global Hemostatic Efficacy Observed

End point title	Global Hemostatic Efficacy Observed[1]
End point description:	
The primary efficacy variable is the hemostatic efficacy as assessed by the Independent Endpoint Adjudication Committee (IEAB). The hemostatic efficacy was assessed based on objective criteria in the categories 'excellent', 'good', 'moderate' or 'none'. Ratings of 'excellent' and 'good' are to be considered as 'effective' hemostasis, while a rating of 'moderate' and 'none' are to be considered as 'ineffective'hemostasis.	
End point type	Primary
End point timeframe:	
At end of the surgery	

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: No statistical analysis for this endpoint.

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	103		
Units: number of patients				
number (not applicable)				
Excellent	41	50		
Good	58	47		
Moderate	6	6		
None	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Non-inferiority Proportion Difference Octaplex vs Kcentra

End point title	Non-inferiority Proportion Difference Octaplex vs Kcentra

End point description:

The dichotomous 'hemostatic success' variable was used in the analyses to demonstrate that treatment with Octaplex was clinically not inferior to treatment with Beriplex® P/N (Kcentra) with respect to hemostatic success. Effective hemostasis includes Excellent and Good ratings, while Ineffective hemostasis includes Moderate and None ratings from Global hemostatic efficacy observed by IEAB. Imputation for Ineffective was performed for missing rating or additional coagulation after initial IP infusion as None.

End point type	Primary

End point timeframe:

At end of the surgery

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	103		
Units: number of patiets				
number (not applicable)				
Effective	99	97		
Ineffective	6	6		

Statistical analyses

Statistical analysis title	Non-inferiority Difference Octaplex vs Kcentra....
Comparison groups	Octaplex v Kcentra
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Farrington’s and Manning’s test
Parameter estimate	Proportion difference
Point estimate	0.001
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.082

Secondary: Patients with an INR value of less or equal to 1.5 at 30 (± 15) minutes after the end of infusion

End point title	Patients with an INR value of less or equal to 1.5 at 30 (± 15) minutes after the end of infusion

End point description:

Proportion of patients with an INR value of less or equal to 1.5 at 30 (± 15) minutes after the end of infusion.

End point type	Secondary

End point timeframe:

30 (± 15) minutes after the end of infusion.

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	103		
Units: patients				
number (not applicable)				
<= 1.5	82	74		
> 1.5	23	29		
Missing	0	0		

Statistical analyses

Statistical analysis title	Proportion difference Octaplex VS Kcentra
Comparison groups	Octaplex v Kcentra
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Proportion difference
Point estimate	0.063
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.056
upper limit	0.181

Notes:

[2] - Farrington's and Manning's test for difference in proportions was performed.

Secondary: Change in Coagulation Factor FII Level

End point title	Change in Coagulation Factor FII Level

End point description:

Change in coagulation factor FII level from baseline to 30 (± 15) minutes after the end of infusion.

End point type	Secondary

End point timeframe:

30 (± 15) minutes after the end of infusion.

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	100[3]		
Units: FII activity (%)				
arithmetic mean (standard deviation)				
Mean baseline	33.7 (± 19.8)	34.4 (± 19.6)		
Mean change from baseline	56.5 (± 29.4)	55.6 (± 28.7)		

Notes:

[3] - Baseline: 101 patients
Change from Baseline: 100 patients

Statistical analyses

Statistical analysis title	Median Difference Octaplex vs Kcentra
Comparison groups	Octaplex v Kcentra
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	9

Secondary: Change in Coagulation Factor FVII Level

End point title	Change in Coagulation Factor FVII Level
End point description:	
Change in coagulation factor FVII level from baseline to 30 (± 15) minutes after the end of infusion.	
End point type	Secondary
End point timeframe:	
30 (± 15) minutes after the end of infusion.	

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	102		
Units: FVII activity (%)				
arithmetic mean (standard deviation)				
Mean baseline	27.6 (± 25.1)	27.3 (± 23.1)		
Mean change from baseline	40.9 (± 32.8)	32.8 (± 34.4)		

Statistical analyses

Statistical analysis title	Median Difference Octaplex vs Kcentra
Comparison groups	Kcentra v Octaplex
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	15

Secondary: Change in Coagulation Factor FIX Level	
End point title	Change in Coagulation Factor FIX Level
End point description: Change in coagulation factor FIX level from baseline to 30 (± 15) minutes after the end of infusion.	
End point type	Secondary
End point timeframe: 30 (± 15) minutes after the end of infusion.	

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	102		
Units: FIX activity (%)				
arithmetic mean (standard deviation)				
Mean baseline	53.0 (± 32.2)	53.6 (± 31.4)		
Mean change from baseline	36.9 (± 37.6)	36.5 (± 33.2)		

Statistical analyses

Statistical analysis title	Median Difference Octaplex vs Kcentra
Comparison groups	Octaplex v Kcentra
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	8

Secondary: Change in Coagulation Factor FX Level

End point title	Change in Coagulation Factor FX Level

End point description:

Change in coagulation factor FX level from baseline to 30 (± 15) minutes after the end of infusion.

End point type	Secondary

End point timeframe:

30 (± 15) minutes after the end of infusion.

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	99[4]		
Units: FX activity (%)				
arithmetic mean (standard deviation)				
Mean baseline	24.4 (± 17.6)	24.0 (± 18.6)		
Mean change from baseline	56.0 (± 29.8)	69.0 (± 32.3)		

Notes:

[4] - Baseline: 100 patients
Change from Baseline: 99 patients

Statistical analyses

Statistical analysis title	Median Difference Octaplex vs Kcentra
Comparison groups	Octaplex v Kcentra
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference
Point estimate	-13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21
upper limit	4

Secondary: Red Blood Cells Received During Surgery

End point title	Red Blood Cells Received During Surgery

End point description:

Proportion of patients receiving red blood cells.

End point type	Secondary

End point timeframe:

during surgery

End point values	Octaplex	Kcentra		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	103		
Units: patients				
number (not applicable)	4	3		

Statistical analyses

Statistical analysis title	Proportion difference Octaplex VS Kcentra
Comparison groups	Octaplex v Kcentra
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Proportion difference
Point estimate	0.009
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.068
upper limit	0.086

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the whole study from baseline up to day 45 (follow up visit)

Adverse event reporting additional description:

AEs were to be followed-up until Day 4. SAEs were to be followed-up until Day 45. If TEEs were suspected at any time during the study, appropriate examinations according to local standards were performed

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Octaplex

Reporting group description:

Patients received 1 Octaplex infusion intravenously

Reporting group title	Kcentra

Reporting group description:

Patients received 1 Kcentra infusions intravenously

Serious adverse events	Octaplex	Kcentra	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 105 (12.38%)	6 / 103 (5.83%)	
number of deaths (all causes)	5	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian cancer stage IV			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to anastomose			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Shock			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic Anaemia			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis erosive			

subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric haematoma			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Soft tissue haemorrhage			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Orchitis			
subjects affected / exposed	1 / 105 (0.95%)	0 / 103 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 105 (0.00%)	1 / 103 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Octaplex	Kcentra	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 105 (80.95%)	80 / 103 (77.67%)	
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 105 (0.00%)	5 / 103 (4.85%)	
occurrences (all)	0	5	
Body temperature increased			
subjects affected / exposed	0 / 105 (0.00%)	4 / 103 (3.88%)	
occurrences (all)	0	4	
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	50 / 105 (47.62%)	50 / 103 (48.54%)	
occurrences (all)	51	50	
Postoperative wound complication			
subjects affected / exposed	15 / 105 (14.29%)	14 / 103 (13.59%)	
occurrences (all)	15	15	
Procedural vomiting			

subjects affected / exposed	4 / 105 (3.81%)	0 / 103 (0.00%)	
occurrences (all)	4	0	
Suture related complication			
subjects affected / exposed	2 / 105 (1.90%)	4 / 103 (3.88%)	
occurrences (all)	2	4	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 105 (0.00%)	3 / 103 (2.91%)	
occurrences (all)	0	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 105 (5.71%)	6 / 103 (5.83%)	
occurrences (all)	6	6	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	13 / 105 (12.38%)	18 / 103 (17.48%)	
occurrences (all)	13	22	
Catheter site related reaction			
subjects affected / exposed	4 / 105 (3.81%)	2 / 103 (1.94%)	
occurrences (all)	5	2	
Hyperthermia			
subjects affected / exposed	3 / 105 (2.86%)	2 / 103 (1.94%)	
occurrences (all)	3	2	
Pyrexia			
subjects affected / exposed	1 / 105 (0.95%)	3 / 103 (2.91%)	
occurrences (all)	1	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 105 (2.86%)	5 / 103 (4.85%)	
occurrences (all)	3	5	
Abdominal distension			
subjects affected / exposed	2 / 105 (1.90%)	3 / 103 (2.91%)	
occurrences (all)	2	3	
Dyschezia			
subjects affected / exposed	1 / 105 (0.95%)	3 / 103 (2.91%)	
occurrences (all)	1	3	

Nausea subjects affected / exposed occurrences (all)	0 / 105 (0.00%) 0	3 / 103 (2.91%) 3	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	5 / 105 (4.76%) 5	2 / 103 (1.94%) 2	
Infections and infestations Pneumonia subjects affected / exposed occurrences (all)	1 / 105 (0.95%) 1	2 / 103 (1.94%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2016	Protocol version 3.0, 21.10.2016: -Additional changes in response to the FDA advice dated October 6, 2016. -ICF revised to align with revised protocol. -Safety section updated to cover post marketing experience of Octaplex use, align with IB ed.10
19 January 2018	Protocol version 4.0, 19.01.2018 - Amendment #1 dated 19-Jan-2018 incorporated: Changes to clarify the text based on the investigators questions and feedback (clarification of ex/in criteria, admin. changes).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 November 2021	The study was conducted in 2 stages, with one un-blinded interim analysis after enrollment of 50% of the planned sample size, to allow for an early stopping of the study for demonstrated non-inferiority of OCTAPLEX or to allow for an early stopping due to futility to achieve this. As study success was claimed on the interim results enrollment of additional patients was prematurely discontinued (as agreed by the FDA on 22-Feb-2022), and this report of the final analysis was prepared. All patients enrolled until a decision to stop the study was made were observed until the end of the follow-up period. The interim analysis was performed by a statistical team which was independent from the study team. The decision to prematurely terminate the study was made in consultation with the relevant authorities.	-

Notes:

Limitations and caveats

None reported