An Open-label, Randomized, Multicenter Phase IIIb Study to Assess the Efficacy, Safety and Tolerance of BERIPLEX® P/N (Kcentra) Compared With Plasma for Rapid Reversal of Coagulopathy Induced by Vitamin K Antagonists in Subjects Requiring an Urgent Surgical Procedure (BE1116_3003)

This study has been completed.

Sponsor:
CSL Behring

Information provided by (Responsible Party):
CSL Behring

ClinicalTrials.gov Identifier:
NCT00803101

First received: December 4, 2008
Last updated: March 18, 2015
Last verified: March 2014
History of Changes

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Results First Received: January 12, 2014

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Reversal of Coagulopathy
Interventions:	Biological: Beriplex® P/N (Kcentra) Biological: Fresh frozen plasma

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline international normalized ratio (INR), amount of coagulation factor IX and body-weight.

Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Participant Flow: Overall Study

	Beriplex® P/N	Fresh Frozen Plasma
STARTED	88	88
COMPLETED	70	66
NOT COMPLETED	18	22
Death / Serious Adverse Event	4	6
Withdrawal by Subject	6	4
Lost to Follow-up	2	2
Protocol Violation	1	7
Surgery finished outside protocol window	1	1
Patient died outside SAE report period	1	0
Patient did not attend scheduled visit	2	1
Patient did not have surgery	1	1

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Intention-to-Treat Efficacy (ITT-E) population included all randomized participants who had received any study product, underwent the intended surgical procedure, and had an INR > 1.3 prior to the infusion. Participants in the ITT-E population were analyzed 'as randomized'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight
Total	Total of all reporting groups

Baseline Measures

	Beriplex® P/N	Fresh Frozen Plasma	Total
Overall Participants [units: participants]	87	81	168
Age, Customized [units: participants]			
< 65 years	32	39	71
>= 65 to < 75 years	21	19	40
>= 75 years	34	23	57
Gender [units: participants]			
Female	37	31	68
Male	50	50	100

Outcome Measures

Hide All Outcome Measures

1. Primary: Percentage of Participants Achieving Hemostatic Efficacy During Surgery [Time Frame: From the start of infusion until the end of surgery]

Measure Type	Primary
Measure Title	Percentage of Participants Achieving Hemostatic Efficacy During Surgery
Measure Description	Hemostatic efficacy was rated as excellent, good, or poor/none, based on prespecified definitions. Hemostatic efficacy was the binary endpoint of effective or non-effective hemostasis, where 'effective' was a hemostatic efficacy rating of "excellent" or "good," and 'non-effective' was a hemostatic efficacy rating of "poor/none".
Time Frame	From the start of infusion until the end of surgery
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Intention-to-Treat Efficacy ITT-E population included all randomized participants who had received any study product, underwent the intended surgical procedure, and had an INR > 1.3 prior to the infusion. Participants in the ITT-E population were analyzed 'as randomized'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Measured Values

	Beriplex® P/N	**Fresh Frozen Plasma**
Overall Participants [units: participants]	**87**	**81**
Percentage of Participants Achieving Hemostatic Efficacy During Surgery [units: percentage of participants] Number (95% Confidence Interval)	**89.7** **(83.3 to 96.1)**	**75.3** **(65.9 to 84.7)**

Statistical Analysis 1 for Percentage of Participants Achieving Hemostatic Efficacy During Surgery

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	95% confidence interval
Difference in effective hemostasis (%) [4]	14.3
95% Confidence Interval	2.8 to 25.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The analysis of hemostatic efficacy was via calculation of the 95% confidence interval (CI) for the difference (Beriplex minus plasma)

	in the percentage of participants with effective hemostasis.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	The non-inferiority margin was −(minus)10%. If the lower limit of the 2-sided 95% CI was >–10%, then the null-hypothesis was rejected and it was concluded that Beriplex was non-inferior to plasma. The sample size estimation assumed that hemostatic efficacy would be rated 'effective' in 85% of participants in the plasma group and 90% of participants in the Beriplex group. The power to show non-inferiority with these assumptions was greater than 80% for two treatment groups of 80 participants.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	The Newcombe-Wilson score method was used to estimate the 95% CI for the difference (Beriplex-plasma) in the % participants with effective hemostasis
[4]	Other relevant estimation information:
	No text entered.

2. Primary: Percentage of Participants Who Had a Rapid Decrease of the INR [Time Frame: 30 minutes after the end of infusion]

Measure Type	Primary
Measure Title	Percentage of Participants Who Had a Rapid Decrease of the INR
Measure Description	A rapid decrease of the INR was defined as an INR ≤ 1.3 at 30 minutes after the end of infusion. The INR is a standard way to describe the time it takes for blood to clot; an INR range of 0.8 to 1.2 is considered normal for a healthy person who is not using oral anticoagulant therapy.
Time Frame	30 minutes after the end of infusion
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT-E population included all randomized participants who had received any study product, underwent the intended surgical procedure, and had an international normalized ratio INR > 1.3 prior to the infusion. Participants in the ITT-E population were analyzed 'as randomized'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Measured Values

	Beriplex® P/N	**Fresh Frozen Plasma**
Overall Participants [units: participants]	**87**	**81**
Percentage of Participants Who Had a Rapid Decrease of the INR [units: percentage of participants] Number (95% Confidence Interval)	**55.2** **(44.7 to 65.6)**	**9.9** **(3.4 to 16.4)**

Statistical Analysis 1 for Percentage of Participants Who Had a Rapid Decrease of the INR

Groups [1]	All groups
Non-Inferiority/Equivalence Test [2]	Yes
Method [3]	Newcombe-Wilson score method
Difference in effective hemostasis (%) [4]	45.3
95% Confidence Interval	31.9 to 56.4

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The analysis of rapid decrease of the INR was via calculation of the 95% CI for the difference (Beriplex minus plasma) in the percentage of participants with INR ≤ 1.3 at 30 minutes after the end of infusion.
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	The non-inferiority margin was −(minus)10%. If the lower limit of the 2-sided 95% CI was >–10%, then the null-hypothesis was rejected and it was concluded that Beriplex was non-inferior to plasma. The sample size estimation assumed that hemostatic efficacy would be rated ‘effective’ in 85% of participants in the plasma group and 90% of participants in the Beriplex group. The power to show non-inferiority with these assumptions was greater than 80% for two treatment groups of 80 participants.
[3]	Other relevant method information, such as adjustments or degrees of freedom:
	The Newcombe-Wilson score method was used to estimate the 95% CI for the difference (Beriplex-plasma) in the % pts with rapid decrease of the INR.
[4]	Other relevant estimation information:
	No text entered.

3. Secondary: Plasma Levels of Factors II, VII, IX, and X, Protein C, and Protein S [Time Frame: From pre-infusion until 24 h after the start of infusion]

Measure Type	Secondary
Measure Title	Plasma Levels of Factors II, VII, IX, and X, Protein C, and Protein S
Measure Description	Plasma levels are presented as the percentage of normal at pre-infusion and 30 min and 24 h after the start of infusion. The plasma level assay results are reported as a potency relative to a standard, where 100% is considered to be normal.
Time Frame	From pre-infusion until 24 h after the start of infusion
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT-E population included all randomized participants who had received any study product, underwent the intended surgical procedure, and had an international normalized ratio INR > 1.3 prior to the infusion. Participants in the ITT-E population were analyzed 'as randomized'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.

Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Measured Values

	Beriplex® P/N	Fresh Frozen Plasma
Overall Participants [units: participants]	**85**	**79**
Plasma Levels of Factors II, VII, IX, and X, Protein C, and Protein S [units: percentage of normal] Mean (Standard Deviation)		
Factor II, pre-infusion (n = 85; 79)	**32.0 (19.93)**	**34.8 (26.19)**
Factor II, 0.5 h after infusion start (n = 71; 73)	**84.5 (20.92)**	**42.5 (25.71)**
Factor II, 24 h after infusion start (n = 81; 74)	**81.4 (24.83)**	**65.6 (23.68)**
Factor VII, pre-infusion start (n = 85; 79)	**36.8 (59.27)**	**31.1 (25.16)**
Factor VII, 0.5h after infusion start (n = 71; 73)	**60.1 (44.91)**	**41.6 (42.90)**
Factor VII, 24 h after infusion start (n = 81; 74)	**85.5 (59.76)**	**83.7 (58.90)**
Factor IX, pre-infusion (n = 85; 79)	**48.1 (25.62)**	**55.8 (30.50)**
Factor IX, 0.5 h after infusion start (n = 71; 73)	**71.6 (25.38)**	**56.2 (23.12)**
Factor IX, 24 h after infusion start (n = 81; 74)	**85.2 (33.39)**	**93.7 (34.25)**
Factor X, pre-infusion (n = 85; 79)	**19.3 (19.32)**	**20.8 (21.38)**
Factor X, 0.5 h after infusion start (n = 71; 73)	**82.3 (23.33)**	**29.8 (22.51)**
Factor X, 24 h after infusion start (n = 81; 74)	**78.3 (25.62)**	**60.2 (22.44)**
Protein C, pre-infusion (n = 85; 78)	**48.8 (19.07)**	**47.6 (21.38)**
Protein C, 0.5 h after infusion start (n = 71; 73)	**97.1 (21.97)**	**52.5 (18.69)**
Protein C, 24 h after infusion start (n = 81; 74)	**87.3 (26.28)**	**78.1 (24.80)**
Protein S, pre-infusion (n = 85; 79)	**45.25 (18.498)**	**46.18 (20.986)**
Protein S, 0.5 h after infusion start (n = 72; 73)	**80.73 (31.489)**	**55.82 (24.689)**
Protein S, 24 h after infusion start (n = 82; 74)	**75.97 (36.449)**	**69.32 (27.504)**

No statistical analysis provided for Plasma Levels of Factors II, VII, IX, and X, Protein C, and Protein S

4. Secondary: Transfusion of Packed Red Blood Cells (PRBCs) or Whole Blood [Time Frame: From the start of surgery until 24 h after the start of surgery]

Measure Type	Secondary
Measure Title	Transfusion of Packed Red Blood Cells (PRBCs) or Whole Blood
Measure Description	The total units of transfused PRBCs or whole blood
Time Frame	From the start of surgery until 24 h after the start of surgery
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT-E population included all randomized participants who had received any study product, underwent the intended surgical procedure, and had an international normalized ratio INR > 1.3 prior to the infusion. Participants in the ITT-E population were analyzed 'as randomized'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Measured Values

	Beriplex® P/N	Fresh Frozen Plasma
Overall Participants [units: participants]	**87**	**81**
Transfusion of Packed Red Blood Cells (PRBCs) or Whole Blood [units: units of PRBCs or whole blood] Mean (Standard Deviation)	**0.3 (0.90)**	**0.4 (1.02)**

No statistical analysis provided for Transfusion of Packed Red Blood Cells (PRBCs) or Whole Blood

5. Secondary: Percentage of Participants With INR Correction at Various Times After the Start of Infusion [Time Frame: From the start of infusion until INR correction; calculated at 0.5, 1, 3, 6, 12, and 24 h after the start of infusion]

Measure Type	Secondary
Measure Title	Percentage of Participants With INR Correction at Various Times After the Start of Infusion
Measure Description	The time taken from the start of infusion to INR correction (defined as an INR ≤ 1.3) was recorded. The percentage of participants with INR correction was calculated at 0.5, 1, 3, 6, 12, and 24 h after the start of infusion.
Time Frame	From the start of infusion until INR correction; calculated at 0.5, 1, 3, 6, 12, and 24 h after the start of infusion
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT-E population included all randomized participants who had received any study product, underwent the intended surgical procedure, and had an international normalized ratio INR > 1.3 prior to the infusion. Participants in the ITT-E population were analyzed 'as randomized'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Measured Values

	Beriplex® P/N	Fresh Frozen Plasma
Overall Participants [units: participants]	**87**	**81**
Percentage of Participants With INR Correction at Various Times After the Start of Infusion [units: percentage of participants]		
0.5 h	**1**	**0**
1 h	**54**	**0**

3 h	**77**	**10**
6 h	**81**	**20**
12 h	**83**	**32**
24 h	**87**	**48**

No statistical analysis provided for Percentage of Participants With INR Correction at Various Times After the Start of Infusion

6. Secondary: Percentage of Participants Who Received Red Blood Cells [Time Frame: From the start of surgery until 24 h after the start of surgery]

Measure Type	Secondary
Measure Title	Percentage of Participants Who Received Red Blood Cells
Measure Description	Red blood cells were PRBCs and whole blood
Time Frame	From the start of surgery until 24 h after the start of surgery
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT-E population included all randomized participants who had received any study product, underwent the intended surgical procedure, and had an international normalized ratio INR > 1.3 prior to the infusion. Participants in the ITT-E population were analyzed 'as randomized'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Measured Values

	Beriplex® P/N	**Fresh Frozen Plasma**
Overall Participants [units: participants]	**87**	**81**
Percentage of Participants Who Received Red Blood Cells [units: percentage of participants]	**16.1**	**14.8**

No statistical analysis provided for Percentage of Participants Who Received Red Blood Cells

7. Secondary: Overall Treatment-emergent Adverse Events (TEAEs) [Time Frame: From the start of infusion up to the allowed time window of the Day 10 visit for non-serious AEs and from the start of infusion up to the allowed time window of the Day 45 visit for SAEs]

Measure Type	Secondary
Measure Title	Overall Treatment-emergent Adverse Events (TEAEs)
Measure Description	Number of participants with TEAEs. TEAEs were defined as adverse events that developed or worsened following exposure to investigational medicinal product. Treatment-related TEAEs were events whose relationship to study

	treatment was related, probably related, or possibly related in the opinion of the investigator. Treatment emergent adverse events with missing relationship were considered related to treatment. Serious TEAEs were treatment-emergent serious adverse events (SAEs).
Time Frame	From the start of infusion up to the allowed time window of the Day 10 visit for non-serious AEs and from the start of infusion up to the allowed time window of the Day 45 visit for SAEs
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Intention-to-Treat Safety (ITT-S) population included all participants who were randomized and who had received any portion of study product. Participants in the ITT-S population were analyzed 'as treated'.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Measured Values

	Beriplex® P/N	**Fresh Frozen Plasma**
Overall Participants [units: participants]	**88**	**88**
Overall Treatment-emergent Adverse Events (TEAEs) [units: participants]		
Any TEAE	**49**	**53**
At least possibly treatment-related TEAE	**8**	**15**
Serious TEAE	**22**	**23**
Death	**4**	**8**

No statistical analysis provided for Overall Treatment-emergent Adverse Events (TEAEs)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	From the start of infusion up to the allowed time window of the Day 10 visit for non-serious AEs and from the start of infusion up to the allowed time window of the Day 45 visit for SAEs.
Additional Description	The AEs presented were serious and non-serious (other) TEAEs. The ITT-S population included all subjects who were randomized and who had received any portion of study product. Participants in the ITT-S population were analyzed 'as treated'. "General disorders" were collected under the MedDRA SOC General disorders and administration site conditions.

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.

Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Serious Adverse Events

	Beriplex® P/N	Fresh Frozen Plasma
Total, serious adverse events		
# participants affected / at risk	**22/88 (25.00%)**	**23/88 (26.14%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**2/88 (2.27%)**	**1/88 (1.14%)**
# events	**2**	**1**
Cardiac disorders		
Acute myocardial infarction † 1		
# participants affected / at risk	**0/88 (0.00%)**	**2/88 (2.27%)**
# events	**0**	**2**
Atrial fibrillation † 1		
# participants affected / at risk	**1/88 (1.14%)**	**1/88 (1.14%)**
# events	**1**	**1**
Cardiac arrest † 1		
# participants affected / at risk	**1/88 (1.14%)**	**1/88 (1.14%)**
# events	**1**	**1**
Cardiac failure congestive † 1		
# participants affected / at risk	**1/88 (1.14%)**	**1/88 (1.14%)**
# events	**1**	**1**
Cardiopulmonary failure † 1		
# participants affected / at risk	**1/88 (1.14%)**	**0/88 (0.00%)**
# events	**1**	**0**
Gastrointestinal disorders		
Gastrointestinal haemorrhage † 1		
# participants affected / at risk	**3/88 (3.41%)**	**0/88 (0.00%)**
# events	**3**	**0**
Upper gastrointestinal haemorrhage † 1		
# participants affected / at risk	**2/88 (2.27%)**	**0/88 (0.00%)**
# events	**3**	**0**
Abdominal pain upper † 1		
# participants affected / at risk	**0/88 (0.00%)**	**1/88 (1.14%)**
# events	**0**	**1**
Intestinal obstruction † 1		
# participants affected / at risk	**1/88 (1.14%)**	**0/88 (0.00%)**
# events	**1**	**0**
Intra-abdominal haematoma † 1		
# participants affected / at risk	**0/88 (0.00%)**	**1/88 (1.14%)**
# events	**0**	**1**
Retroperitoneal haemorrhage † 1		
# participants affected / at risk	**1/88 (1.14%)**	**0/88 (0.00%)**
# events	**1**	**0**
General disorders		
Death † 1		

# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Systemic inflammatory response syndrome † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Wound necrosis † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Hepatobiliary disorders		
Cholecystitis acute † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Infections and infestations		
Pneumonia † 1		
# participants affected / at risk	0/88 (0.00%)	3/88 (3.41%)
# events	0	3
Sepsis † 1		
# participants affected / at risk	0/88 (0.00%)	2/88 (2.27%)
# events	0	2
Bronchopneumonia † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Clostridium difficile colitis † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Septic shock † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Urinary tract infection † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Urosepsis † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Injury, poisoning and procedural complications		
Post procedural discharge † 1		
# participants affected / at risk	1/88 (1.14%)	1/88 (1.14%)
# events	1	1
Subdural haematoma † 1		
# participants affected / at risk	1/88 (1.14%)	1/88 (1.14%)
# events	1	1
Post procedural haemorrhage † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Vena cava injury † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Metabolism and nutrition disorders		

Hypoglycaemia † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Musculoskeletal and connective tissue disorders		
Soft tissue necrosis † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Lung carcinoma cell type unspecified stage IV † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Tumor haemorrhage † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Nervous system disorders		
Coma † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Dementia † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Embolic cerebral infarction † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Encephalopathy † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Ischaemic stroke † 1		
# participants affected / at risk	1/88 (1.14%)	0/88 (0.00%)
# events	1	0
Subarachnoid haemorrhage † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
Renal and urinary disorders		
Renal failure acute † 1		
# participants affected / at risk	2/88 (2.27%)	0/88 (0.00%)
# events	2	0
Respiratory, thoracic and mediastinal disorders		
Respiratory failure † 1		
# participants affected / at risk	1/88 (1.14%)	3/88 (3.41%)
# events	1	3
Pneumonia aspiration † 1		
# participants affected / at risk	1/88 (1.14%)	1/88 (1.14%)
# events	1	1
Acute pulmonary oedema † 1		
# participants affected / at risk	0/88 (0.00%)	1/88 (1.14%)
# events	0	1
† 1		

Acute respiratory failure		
# participants affected / at risk	**1/88 (1.14%)**	**0/88 (0.00%)**
# events	**1**	**0**
Pleural effusion † 1		
# participants affected / at risk	**0/88 (0.00%)**	**1/88 (1.14%)**
# events	**0**	**1**
Pulmonary embolism † 1		
# participants affected / at risk	**0/88 (0.00%)**	**1/88 (1.14%)**
# events	**0**	**1**
Surgical and medical procedures		
Wound drainage † 1		
# participants affected / at risk	**1/88 (1.14%)**	**0/88 (0.00%)**
# events	**1**	**0**
Vascular disorders		
Deep vein thrombosis † 1		
# participants affected / at risk	**1/88 (1.14%)**	**1/88 (1.14%)**
# events	**1**	**1**
Haematoma † 1		
# participants affected / at risk	**0/88 (0.00%)**	**1/88 (1.14%)**
# events	**0**	**1**
Shock † 1		
# participants affected / at risk	**0/88 (0.00%)**	**1/88 (1.14%)**
# events	**0**	**1**
Thrombosis † 1		
# participants affected / at risk	**1/88 (1.14%)**	**0/88 (0.00%)**
# events	**1**	**0**
Venous insufficiency † 1		
# participants affected / at risk	**1/88 (1.14%)**	**0/88 (0.00%)**
# events	**1**	**0**
Hypertension † 1		
# participants affected / at risk	**0/88 (0.00%)**	**1/88 (1.14%)**
# events	**0**	**1**

† Events were collected by systematic assessment

1 Term from vocabulary, MedDRA V12.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	From the start of infusion up to the allowed time window of the Day 10 visit for non-serious AEs and from the start of infusion up to the allowed time window of the Day 45 visit for SAEs.
Additional Description	The AEs presented were serious and non-serious (other) TEAEs. The ITT-S population included all subjects who were randomized and who had received any portion of study product. Participants in the ITT-S population were analyzed 'as treated'. "General disorders" were collected under the MedDRA SOC General disorders and administration site conditions.

Frequency Threshold

Threshold above which other adverse events are reported	2

Reporting Groups

	Description
Beriplex® P/N	Beriplex® P/N: Intravenous infusion, dosage depending on baseline INR, amount of coagulation factor IX and body-weight.
Fresh Frozen Plasma	Fresh frozen plasma: Intravenous infusion, dosage depending on baseline INR and body weight

Other Adverse Events

	Beriplex® P/N	Fresh Frozen Plasma
Total, other (not including serious) adverse events		
# participants affected / at risk	**41/88 (46.59%)**	**44/88 (50.00%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**9/88 (10.23%)**	**9/88 (10.23%)**
# events	**9**	**9**
Thrombocytopenia † 1		
# participants affected / at risk	**2/88 (2.27%)**	**2/88 (2.27%)**
# events	**2**	**2**
Haemorrhagic anaemia † 1		
# participants affected / at risk	**2/88 (2.27%)**	**1/88 (1.14%)**
# events	**2**	**1**
Cardiac disorders		
Atrial fibrillation † 1		
# participants affected / at risk	**5/88 (5.68%)**	**3/88 (3.41%)**
# events	**6**	**3**
Tachycardia † 1		
# participants affected / at risk	**5/88 (5.68%)**	**1/88 (1.14%)**
# events	**5**	**1**
Cardiac failure congestive † 1		
# participants affected / at risk	**2/88 (2.27%)**	**2/88 (2.27%)**
# events	**2**	**2**
Ventricular tachycardia † 1		
# participants affected / at risk	**1/88 (1.14%)**	**2/88 (2.27%)**
# events	**1**	**2**
Ventricular extrasystoles † 1		
# participants affected / at risk	**2/88 (2.27%)**	**0/88 (0.00%)**
# events	**2**	**0**
Gastrointestinal disorders		
Constipation † 1		
# participants affected / at risk	**10/88 (11.36%)**	**4/88 (4.55%)**
# events	**10**	**4**
Nausea † 1		
# participants affected / at risk	**7/88 (7.95%)**	**4/88 (4.55%)**
# events	**7**	**4**
Diarrhoea † 1		
# participants affected / at risk	**3/88 (3.41%)**	**3/88 (3.41%)**
# events	**3**	**3**
Dysphagia † 1		

# participants affected / at risk	1/88 (1.14%)	2/88 (2.27%)
# events	1	2
Vomiting † 1		
# participants affected / at risk	2/88 (2.27%)	1/88 (1.14%)
# events	2	1
General disorders		
Oedema peripheral † 1		
# participants affected / at risk	6/88 (6.82%)	6/88 (6.82%)
# events	6	6
Pyrexia † 1		
# participants affected / at risk	3/88 (3.41%)	5/88 (5.68%)
# events	3	5
Infections and infestations		
Urinary tract infection † 1		
# participants affected / at risk	1/88 (1.14%)	3/88 (3.41%)
# events	1	3
Pneumonia † 1		
# participants affected / at risk	2/88 (2.27%)	0/88 (0.00%)
# events	2	0
Injury, poisoning and procedural complications		
Incision site pain † 1		
# participants affected / at risk	1/88 (1.14%)	3/88 (3.41%)
# events	1	3
Contusion † 1		
# participants affected / at risk	1/88 (1.14%)	2/88 (2.27%)
# events	1	2
Skin laceration † 1		
# participants affected / at risk	2/88 (2.27%)	1/88 (1.14%)
# events	2	1
Investigations		
Body temperature increased † 1		
# participants affected / at risk	3/88 (3.41%)	1/88 (1.14%)
# events	3	1
Blood glucose increased † 1		
# participants affected / at risk	2/88 (2.27%)	0/88 (0.00%)
# events	2	0
Metabolism and nutrition disorders		
Hypokalaemia † 1		
# participants affected / at risk	7/88 (7.95%)	8/88 (9.09%)
# events	7	9
Hypocalcaemia † 1		
# participants affected / at risk	4/88 (4.55%)	3/88 (3.41%)
# events	4	3
Hyperglycaemia † 1		
# participants affected / at risk	3/88 (3.41%)	2/88 (2.27%)
# events	3	2
Decreased appetite † 1		
# participants affected / at risk	1/88 (1.14%)	2/88 (2.27%)

# events	1	2
Fluid overload † 1		
# participants affected / at risk	0/88 (0.00%)	3/88 (3.41%)
# events	0	3
Dehydration † 1		
# participants affected / at risk	2/88 (2.27%)	0/88 (0.00%)
# events	2	0
Musculoskeletal and connective tissue disorders		
Muscle spasms † 1		
# participants affected / at risk	2/88 (2.27%)	1/88 (1.14%)
# events	2	1
Pain in extremity † 1		
# participants affected / at risk	1/88 (1.14%)	2/88 (2.27%)
# events	1	3
Joint swelling † 1		
# participants affected / at risk	2/88 (2.27%)	0/88 (0.00%)
# events	2	0
Nervous system disorders		
Headache † 1		
# participants affected / at risk	3/88 (3.41%)	3/88 (3.41%)
# events	3	3
Tremor † 1		
# participants affected / at risk	2/88 (2.27%)	0/88 (0.00%)
# events	2	0
Psychiatric disorders		
Insomnia † 1		
# participants affected / at risk	3/88 (3.41%)	3/88 (3.41%)
# events	3	3
Confusional state † 1		
# participants affected / at risk	3/88 (3.41%)	2/88 (2.27%)
# events	4	2
Agitation † 1		
# participants affected / at risk	2/88 (2.27%)	2/88 (2.27%)
# events	2	2
Renal and urinary disorders		
Urinary retention † 1		
# participants affected / at risk	1/88 (1.14%)	3/88 (3.41%)
# events	1	3
Haematuria † 1		
# participants affected / at risk	2/88 (2.27%)	1/88 (1.14%)
# events	2	1
Respiratory, thoracic and mediastinal disorders		
Pulmonary oedema † 1		
# participants affected / at risk	1/88 (1.14%)	5/88 (5.68%)
# events	1	5
Hypoxia † 1		
# participants affected / at risk	2/88 (2.27%)	2/88 (2.27%)

# events	2	2
Pleural effusion † 1		
# participants affected / at risk	3/88 (3.41%)	1/88 (1.14%)
# events	3	1
Productive cough † 1		
# participants affected / at risk	4/88 (4.55%)	0/88 (0.00%)
# events	4	0
Atelectasis † 1		
# participants affected / at risk	2/88 (2.27%)	1/88 (1.14%)
# events	2	1
Cough † 1		
# participants affected / at risk	2/88 (2.27%)	1/88 (1.14%)
# events	2	1
Dyspnoea † 1		
# participants affected / at risk	0/88 (0.00%)	3/88 (3.41%)
# events	0	3
Rales † 1		
# participants affected / at risk	0/88 (0.00%)	2/88 (2.27%)
# events	0	3
Skin and subcutaneous tissue disorders		
Decubitus ulcer † 1		
# participants affected / at risk	3/88 (3.41%)	1/88 (1.14%)
# events	3	1
Erythema † 1		
# participants affected / at risk	2/88 (2.27%)	2/88 (2.27%)
# events	3	2
Pruritis † 1		
# participants affected / at risk	2/88 (2.27%)	1/88 (1.14%)
# events	2	1
Rash † 1		
# participants affected / at risk	3/88 (3.41%)	0/88 (0.00%)
# events	3	0
Vascular disorders		
Hypotension † 1		
# participants affected / at risk	7/88 (7.95%)	6/88 (6.82%)
# events	7	6

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA V12.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: CSL agreements and restrictions on publishing may vary with individual investigators; however, CSL will not prohibit any investigator from publishing. CSL supports the publication of results from all centers of a multi-center trial and generally requires that reports based on single-site data not precede the primary publication of the entire clinical trial.

Results Point of Contact:

Name/Title: Clinical Trial Disclosure Manager
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e-mail: clinicaltrials@cslbehring.com

Publications of Results:

Goldstein JN, Refaai MA, Milling TJ Jr, Lewis B, Goldberg-Alberts R, Hug BA, Sarode R. Four-factor prothrombin complex concentrate versus plasma for rapid vitamin K antagonist reversal in patients needing urgent surgical or invasive interventions: a phase 3b, open-label, non-inferiority, randomised trial. Lancet. 2015 May 23;385(9982):2077-87. doi: 10.1016/S0140-6736(14)61685-8.

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Refaai MA, Goldstein JN, Lee ML, Durn BL, Milling TJ Jr, Sarode R. Increased risk of volume overload with plasma compared with four-factor prothrombin complex concentrate for urgent vitamin K antagonist reversal. Transfusion. 2015 Nov;55(11):2722-9. doi: 10.1111/trf.13191.

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