Clinical trial results:
Safety and efficacy of subcutaneous (SC) administration of Clinimix N9G15E in elderly patients at risk for malnutrition, at a dose of 1 liter infused over 12 hours for 7 to 10 consecutive days. A prospective, multicentre, randomized, open-label, non-inferiority, controlled phase III B trial carried out in parallel groups: subcutaneous versus peripheral intravenous administration.

Summary

EudraCT number	2007-006153-31
Trial protocol	FR
Global end of trial date	09 April 2010

Results information

Result version number	v1 (current)
This version publication date	21 April 2018
First version publication date	21 April 2018

Trial information

Trial identification

Sponsor protocol code	CSC/P01/07/Mu.F

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Baxter Healthcare Corporation
Sponsor organisation address	1 Baxter Parkway, Deerfield, United States, 60015
Public contact	Clinical Trials Disclosure Call Center, Baxter Healthcare Corporation, Global_CORP_ClinicalTrialsDisclosure@baxter.com
Scientific contact	Clinical Trials Disclosure Call Center, Baxter Healthcare Corporation, Global_CORP_ClinicalTrialsDisclosure@baxter.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	09 April 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 April 2010
Global end of trial reached?	Yes
Global end of trial date	09 April 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate that the SC administration of 1 liter of Clinimix N9G15E is non-inferior to the peripheral IV administration of 1 liter of Clinimix N9g15E in terms of local side effects. The secondary objective was to assess safety and efficacy in terms of patients' nutritional parameters, clinical outcomes, and hydration status.

Protection of trial subjects:

A patient could withdraw consent at any time for any reason. Patients were discontinued from the study if any of the following occurred during the course of the study:
-Patient required enteral or other parenteral administration.
-Patient or patient's legal authorized representative withdrew consent.
-Patient enrolled in any other investigational study.
-Onset of any serious or life threatening adverse event requiring discontinuation of study treatment.
-Investigator's decision.
-In case of the need for a second administration route switch.
-Patient required therapeutic anticoagulation after enrollment in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 July 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 120
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	0
From 65 to 84 years	100
85 years and over	20

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study population (geriatric) chosen represented one population with difficult venous access and where SC hydration has been effective. The population contained patients with many different disorders. Other populations with difficult venous access may benefit from the therapy (the study was not meant to be exclusive of other populations).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SC Treatment

Arm description:

Subcutaneous (SC) Treatment of Clinimix N9G15E at a dose of 1 liter was infused subcutaneously over 12 hours for at least 7 and up to 10 consecutive days. Infusion sites included abdominal area, thighs, back and chest and were to be changed after administration of each 1 liter bag. Subcutaneous infusions were administered with a 21 to 25 G butterfly needle or catheter.

Arm type	Experimental
Investigational medicinal product name	Clinimix N9G15E Subcutaneous
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

The Clinimix N9G15E 1 L bag contained 27.5 g amino acids with electrolytes (Na, K, Ca, Mg, and PO4) and 75 g glucose, in separate chambers, providing a total of 410 kcal/L. The final osmolarity (after mixing) was 845 mOsm/L. All 1000 mL were planned to be infused over 12 hours, resulting in a rate of infusion of approximately 83 to 84 mL/hour, not exceeding a rate of 3 mL/kg/hour.

Arm title	IV Treatment

Arm description:

Intravenous (IV) Treatment of Clinimix N9G15E at a dose of 1 liter was infused via peripheral IV over 12 hours for at least 7 and up to 10 consecutive days. Peripheral IV drips were to be changed by the local implementation of the local Comite' de Liaison en Alimentation et Nutrition (CLAN) recommendations. The peripheral IV lines used for administration of Clinimix were to be used only for administration of the study test product. After administration of the final dose of test product, the peripheral IV line was to be removed and the injection site was not to be used for 48 hours.

Arm type	Active comparator
Investigational medicinal product name	Clinimix N9G15E Intravenous
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

The Clinimix N9G15E 1 L bag contained 27.5 g amino acids with electrolytes (Na, K, Ca, Mg, and PO4) and 75 g glucose, in separate chambers, providing a total of 410 kcal/L. The final osmolarity (after mixing) was 845 mOsm/L. All 1000 mL were planned to be infused over 12 hours, resulting in a rate of infusion of approximately 83 to 84 mL/hour, not exceeding a rate of 3 mL/kg/hour.

Number of subjects in period 1	SC Treatment	IV Treatment
Started	59	61
Completed	49	53
Not completed	10	8
Consent withdrawn by subject	3	1
Clinical adverse event	3	3
Deaths	1	1
Unknown	2	1
Protocol Noncompliance	-	1
Biological adverse event	1	1

Baseline characteristics

Reporting groups	
Reporting group title	SC Treatment
Reporting group description:	
Subcutaneous (SC) Treatment of Clinimix N9G15E at a dose of 1 liter was infused subcutaneously over 12 hours for at least 7 and up to 10 consecutive days. Infusion sites included abdominal area, thighs, back and chest and were to be changed after administration of each 1 liter bag. Subcutaneous infusions were administered with a 21 to 25 G butterfly needle or catheter.	
Reporting group title	IV Treatment
Reporting group description:	
Intravenous (IV) Treatment of Clinimix N9G15E at a dose of 1 liter was infused via peripheral IV over 12 hours for at least 7 and up to 10 consecutive days. Peripheral IV drips were to be changed by the local implementation of the local Comite' de Liaison en Alimentation et Nutrition (CLAN) recommendations. The peripheral IV lines used for administration of Clinimix were to be used only for administration of the study test product. After administration of the final dose of test product, the peripheral IV line was to be removed and the injection site was not to be used for 48 hours.	

Reporting group values	SC Treatment	IV Treatment	Total
Number of subjects	59	61	120
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	84.4	84.9	
standard deviation	± 6.14	± 5.92	-
Gender categorical Units: Subjects			
Female	34	44	78
Male	25	17	42

End points

End points reporting groups

Reporting group title	SC Treatment

Reporting group description:

Subcutaneous (SC) Treatment of Clinimix N9G15E at a dose of 1 liter was infused subcutaneously over 12 hours for at least 7 and up to 10 consecutive days. Infusion sites included abdominal area, thighs, back and chest and were to be changed after administration of each 1 liter bag. Subcutaneous infusions were administered with a 21 to 25 G butterfly needle or catheter.

Reporting group title	IV Treatment

Reporting group description:

Intravenous (IV) Treatment of Clinimix N9G15E at a dose of 1 liter was infused via peripheral IV over 12 hours for at least 7 and up to 10 consecutive days. Peripheral IV drips were to be changed by the local implementation of the local Comite' de Liaison en Alimentation et Nutrition (CLAN) recommendations. The peripheral IV lines used for administration of Clinimix were to be used only for administration of the study test product. After administration of the final dose of test product, the peripheral IV line was to be removed and the injection site was not to be used for 48 hours.

Primary: Number of Patients with at Least One Major Local Side Effect

End point title	Number of Patients with at Least One Major Local Side Effect

End point description:

Major local side effects were evaluated before the start of and at the end of an infusion. An event reported at the start of an infusion was allocated to the route of the previous administration as the "12 hour later" assessment. If an AE occurred before a change/switch of administration route, it was attributed to the previous route. The event was considered a major local side effect if, during the infusion that the major local side effect was attributed to, the subject was infused with a least 800mL of study product and the infusion was between 8 and 16 hours in duration. This endpoint was defined as the occurrence of at least 1 of the following: large edema (diameter>10cm); blistering (diameter>2cm); erythema (diameter>10cm); phlebitis; cellulitis; or strong (unbearable) pain.

End point type	Primary

End point timeframe:

Day 1 to Day 11

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Patients				
number (not applicable)	16	27		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.059
Method	Fisher exact
Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	0.4

Primary: Number of Patients by Major Local Side Effect Type	
End point title	Number of Patients by Major Local Side Effect Type
End point description: Large edema (diameter > 10 cm) Blistering (diameter > 2 cm) Erythema (diameter > 10 cm)	
End point type	Primary
End point timeframe: Day 1 to Day 11	

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Patients				
number (not applicable)				
Large edema	13	5		
Blistering	0	0		
Erythema	5	2		
Unbearable pain	0	1		
Phlebitis	1	0		
Cellulitis	1	1		

Statistical analyses

Statistical analysis title	Large edema
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.042
Method	Fisher exact

Statistical analysis title	Erythema
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.268
Method	Fisher exact

Statistical analysis title	Unbearable pain
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Fisher exact

Statistical analysis title	Phlebitis
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.492
Method	Fisher exact

Statistical analysis title	Cellulitis
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1
Method	Fisher exact

Secondary: Change from Baseline in Body Weight at End of Treatment	
End point title	Change from Baseline in Body Weight at End of Treatment
End point description:	

End point type	Secondary
End point timeframe:	
Baseline to End of Treatment (Day 11)	

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Kilogram (kg)				
arithmetic mean (standard deviation)	0.8 (± 2.26)	0.4 (± 1.60)		

Statistical analyses

Statistical analysis title	Stats 1
Statistical analysis description: Difference from Baseline to End of Treatment	
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.453
Method	F-test

Secondary: Change from Baseline in Body Mass Index (BMI) at End of Treatment

End point title	Change from Baseline in Body Mass Index (BMI) at End of Treatment
End point description:	
End point type	Secondary
End point timeframe: Baseline and End of Treatment (Day 11)	

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: kg/m2				
arithmetic mean (standard deviation)	0.4 (± 0.94)	0.2 (± 0.62)		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.465
Method	F-test

Secondary: Change from Baseline in Transthyretin at End of Treatment

End point title	Change from Baseline in Transthyretin at End of Treatment

End point description:

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Day 11)

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: g/L				
arithmetic mean (standard deviation)	0.02 (± 0.038)	0.01 (± 0.048)		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.26
Method	F-test

Secondary: Change from Baseline in Albumin at End of Treatment

End point title	Change from Baseline in Albumin at End of Treatment

End point description:

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Day 11)

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: g/L				
arithmetic mean (standard deviation)	0 (± 3.6)	-0 (± 3.3)		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.854
Method	F-test

Secondary: Change from Baseline in Transferrin at End of Treatment

End point title	Change from Baseline in Transferrin at End of Treatment

End point description:

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Day 11)

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: umol/L				
arithmetic mean (standard deviation)	2.1 (± 3.1)	0.4 (± 4.5)		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.17
Method	F-test

Secondary: Change from Baseline in Lymphocytes at End of Treatment

End point title	Change from Baseline in Lymphocytes at End of Treatment

End point description:

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Day 11)

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: cells/mm3				
arithmetic mean (standard deviation)	-11 (± 533.1)	-69 (± 368.7)		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.567
Method	f-test

Secondary: Change from Baseline in Clinical Laboratory Hydration Parameters

End point title	Change from Baseline in Clinical Laboratory Hydration Parameters

End point description:

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Day 11)

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: mmol/L				
arithmetic mean (standard deviation)				
Potassium	0.24 (± 0.494)	0.23 (± 0.397)		
Chloride	0.0 (± 3.3)	0 (± 9.9)		
Bicarbonate	-0.4 (± 3.28)	0.7 (± 4.67)		
Calcium	0.04 (± 0.188)	0 (± 0.096)		
Magnesium	0.05 (± 0.089)	0.05 (± 0.082)		
Phosphorus	0.13 (± 0.245)	0.09 (± 0.184)		
Glucose	0.12 (± 2.244)	0.61 (± 2.112)		

Statistical analyses

Statistical analysis title	Potassium
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.63
Method	F-test

Statistical analysis title	Chloride
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.576
Method	F-test

Statistical analysis title	Bicarbonate
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.27
Method	F-test

Statistical analysis title	Calcium
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.611
Method	F-test

Statistical analysis title	Magnesium
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.935
Method	F-test

Statistical analysis title	Phosphorus
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.508
Method	F-test

Statistical analysis title	Glucose
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.386
Method	F-test

Secondary: Adherence (by Days) to Assigned Administration Route	
End point title	Adherence (by Days) to Assigned Administration Route

End point description:

Adherence to assigned administration route is defined as the number of days before any change/switch of administration route for patients who did experience a change/switch, or the total duration of treatment in days for patients who did not experience a change/switch.

End point type	Secondary

End point timeframe:

Day 1 to Day 11

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Days				
arithmetic mean (standard deviation)	7.4 (± 2.4)	5.6 (± 3)		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	F-test

Secondary: Length of Stay until Date of Discharge

End point title	Length of Stay until Date of Discharge

End point description:

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Day 11)

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Days				
arithmetic mean (standard deviation)	21.3 (± 13.2)	20.8 (± 13.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Length of Stay until Date Ready for Discharge

End point title	Length of Stay until Date Ready for Discharge

End point description:

End point type	Secondary

End point timeframe:

Baseline and End of Treatment (Day 11)

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Days				
arithmetic mean (standard deviation)	20.2 (± 13.3)	22.3 (± 16.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients by Destination at Discharge

End point title	Percentage of Patients by Destination at Discharge

End point description:

End point type	Secondary

End point timeframe:

Day 21/End of Study

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Destination (location)				
number (not applicable)				
Home	32.2	24.6		
Nursing Home	15.3	14.8		
Chronic Care Facility	15.3	11.5		
Other	28.8	39.3		
Remain in Ward	0	0		
Unknown	8.5	9.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Survival at End of Study

End point title	Patient Survival at End of Study

End point description:

End point type	Secondary

End point timeframe:

Day 21/End of Study

End point values	SC Treatment	IV Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	61		
Units: Patients				
number (not applicable)				
Deaths	3	5		
Censored	56	56		

Statistical analyses

Statistical analysis title	Stats 1
Comparison groups	SC Treatment v IV Treatment
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Hazard ratio (HR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	11.9

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment Emergent	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11

Reporting groups	
Reporting group title	SC Before or During Switch or Route
Reporting group description: -	
Reporting group title	IV Before or During Switch or Route
Reporting group description: -	
Reporting group title	SC after switch of route
Reporting group description: -	

Serious adverse events	SC Before or During Switch or Route	IV Before or During Switch or Route	SC after switch of route
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 61 (11.48%)	6 / 59 (10.17%)	3 / 21 (14.29%)
number of deaths (all causes)	3	4	1
number of deaths resulting from adverse events	3	4	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL CANCER			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL CARCINOMA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Injury, poisoning and procedural complications			
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			

ARTERIAL DISORDER			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
THROMBOPHLEBITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
General disorders and administration site conditions			
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 61 (1.64%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Respiratory, thoracic and mediastinal disorders			
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL FAILURE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL FAILURE ACUTE			

subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
PNEUMONIA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metabolism and nutrition disorders			
DIABETES MELLITUS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERKALAEMIA			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	SC Before or During Switch or Route	IV Before or During Switch or Route	SC after switch of route
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 61 (68.85%)	37 / 59 (62.71%)	11 / 21 (52.38%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL CANCER			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
OESOPHAGEAL CARCINOMA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0

Vascular disorders			
ARTERIAL DISORDER			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
POOR VENOUS ACCESS			
subjects affected / exposed	0 / 61 (0.00%)	4 / 59 (6.78%)	0 / 21 (0.00%)
occurrences (all)	0	4	0
THROMBOPHLEBITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 61 (1.64%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences (all)	1	2	0
HYPERTHERMIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
INFLAMMATION			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
INFUSION SITE CELLULITIS			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
INFUSION SITE ERYTHEMA			
subjects affected / exposed	5 / 61 (8.20%)	3 / 59 (5.08%)	0 / 21 (0.00%)
occurrences (all)	8	3	0
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
INFUSION SITE HAEMATOMA			

subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
INFUSION SITE INFLAMMATION			
subjects affected / exposed	0 / 61 (0.00%)	8 / 59 (13.56%)	0 / 21 (0.00%)
occurrences (all)	0	9	0
INFUSION SITE OEDEMA			
subjects affected / exposed	19 / 61 (31.15%)	7 / 59 (11.86%)	5 / 21 (23.81%)
occurrences (all)	42	7	11
INFUSION SITE PAIN			
subjects affected / exposed	1 / 61 (1.64%)	3 / 59 (5.08%)	2 / 21 (9.52%)
occurrences (all)	1	5	2
INFUSION SITE REACTION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
INFUSION SITE VESICLES			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
PYREXIA			
subjects affected / exposed	2 / 61 (3.28%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences (all)	2	2	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
EPISTAXIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
LUNG DISORDER			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
PULMONARY EMBOLISM			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Investigations			
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
BLOOD UREA INCREASED			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
THYROXINE FREE INCREASED			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
DUST INHALATION PNEUMOPATHY			
subjects affected / exposed	2 / 61 (3.28%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0

FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
SYNCOPE			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
CARDIAC DISORDERS			
subjects affected / exposed	1 / 61 (1.64%)	3 / 59 (5.08%)	1 / 21 (4.76%)
occurrences (all)	1	3	1
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
CARDIAC FAILURE			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	1 / 21 (4.76%)
occurrences (all)	0	1	1
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
CONJUNCTIVITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			

subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
CONSTIPATION			
subjects affected / exposed	2 / 61 (3.28%)	0 / 59 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	2
DIARRHOEA			
subjects affected / exposed	4 / 61 (6.56%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences (all)	4	2	0
NAUSEA			
subjects affected / exposed	1 / 61 (1.64%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences (all)	1	2	0
VOMITING			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
MUCOCUTANEOUS RASH			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
RENAL FAILURE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
RENAL FAILURE ACUTE			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
URINARY RETENTION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 61 (1.64%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
MUSCLE SPASMS			

subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
NECK PAIN			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
ERYSIPELAS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
FUNGAL INFECTION			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
GASTROENTERITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
HELICOBACTER GASTRITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
LYMPHANGITIS			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
PNEUMONIA			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
PYELONEPHRITIS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
SEPTIC SHOCK			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
SKIN INFECTION			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0

URINARY TRACT INFECTION			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	2	1	0
DIABETES MELLITUS			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
HYPERKALAEMIA			
subjects affected / exposed	2 / 61 (3.28%)	0 / 59 (0.00%)	1 / 21 (4.76%)
occurrences (all)	2	0	1
HYPOKALAEMIA			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
HYPONATRAEMIA			
subjects affected / exposed	2 / 61 (3.28%)	2 / 59 (3.39%)	0 / 21 (0.00%)
occurrences (all)	2	2	0
MALNUTRITION			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 21 (0.00%)
occurrences (all)	0	1	0

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