Clinical trial results:
A multicentre, double blind, randomized placebo controlled trial to assess the effect of LF-PB on seroma formation in women with breast cancer undergoing Axillary Lymph Node Dissection

Summary

EudraCT number	2014-005289-31
Trial protocol	IT
Global end of trial date	19 July 2016

Results information

Result version number	v1 (current)
This version publication date	24 May 2020
First version publication date	24 May 2020

Trial information

Trial identification

Sponsor protocol code	LF-PB/14/05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02668588
WHO universal trial number (UTN)	-
Other trial identifiers	ND: ND

Notes:

Sponsors

Sponsor organisation name	Chemi S.p.A.
Sponsor organisation address	Via dei Lavoratori 54, Cinisello Balsamo, MI, Italy, 20092
Public contact	Clinical Research and Development Director, Chemi S.p.A, +39 02 6443 1, p.bettica@italfarmaco.com
Scientific contact	Clinical Research and Development Director, Chemi S.p.A, +39 02 64431, p.bettica@italfarmaco.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	19 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 July 2016
Global end of trial reached?	Yes
Global end of trial date	19 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives were:
• To assess the effect of LF-PB 30 mg versus placebo on seroma incidence by Day 28 after ALND.
• To assess the safety and tolerability of LF-PB 30 mg.

Protection of trial subjects:

The trial was conducted in accordance with the Helsinki Declaration and the International Council for Harmonisation (ICH) guidelines on Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 October 2015
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	Italy: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	32
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who signed the inform consent to participate in this trial underwent screening assessments within 3 weeks from Day 0 (randomization/the day of surgery).

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	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Blinding implementation details:

This was a double-blind study. No further details on the blinding implemetation are reported in the CSR/protocol of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	LF-PB 30 mg

Arm description:

LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Arm type	Experimental
Investigational medicinal product name	LF-PB
Investigational medicinal product code	
Other name	octreotide acetate
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

Subjects were dosed once with 30 mg LF-PB administered via gluteus bolus injection. Formulation: Reconstituted active product for i.m. administration. LF-PB 30 mg was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v)

Arm title	Placebo

Arm description:

Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

Subjects were dosed once with placebo for LF-PB 30 mg: administered via gluteus bolus injection. Formulation: reconstituted placebo product for i.m. administration. Placebo for LF-PB 30 mg was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-

cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Number of subjects in period 1	LF-PB 30 mg	Placebo
Started	24	24
Completed	22	24
Not completed	2	0
Consent withdrawn by subject	2	-

Baseline characteristics

Reporting groups

Reporting group title	LF-PB 30 mg

Reporting group description:

LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Reporting group title	Placebo

Reporting group description:

Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Reporting group values	LF-PB 30 mg	Placebo	Total
Number of subjects	24	24	48
Age categorical Units: Subjects			
Adults (18-64 years)	16	17	33
From 65-84 years	8	7	15
Gender categorical			
In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled.			
Units: Subjects			
Female	24	24	48

Subject analysis sets

Subject analysis set title	LF-PB 30 mg - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained.

Subject analysis set title	Placebo - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained.

Subject analysis set title	LF-PB 30 mg - safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used to summarize the safety assessments.

Subject analysis set title	Placebo - safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used

to summarize the safety assessments.

Subject analysis set title	LF-PB 30 mg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK population: The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic

Subject analysis set title	placebo - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic

Subject analysis set title	LF-PB 30 mg - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

Subject analysis set title	placebo - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

Reporting group values	LF-PB 30 mg - ITT population	Placebo - ITT population	LF-PB 30 mg - safety population
Number of subjects	24	24	24
Age categorical Units: Subjects			
Adults (18-64 years)	16	17	16
From 65-84 years	8	7	8
Gender categorical			
In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled.			
Units: Subjects			
Female	24	24	24

Reporting group values	Placebo - safety population	LF-PB 30 mg - PK population	placebo - PK population
Number of subjects	24	24	24
Age categorical Units: Subjects			
Adults (18-64 years)	17	16	17
From 65-84 years	7	8	7
Gender categorical			
In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled.			
Units: Subjects			
Female	24	24	24

Reporting group values	LF-PB 30 mg - PP population	placebo - PP population	
Number of subjects	23	23	
Age categorical Units: Subjects			
Adults (18-64 years) From 65-84 years			
Gender categorical			
In this study only females aged ≥ 18 years who underwent breast cancer surgery with axillary lymph node dissection were enrolled.			
Units: Subjects			
Female			

End points

End points reporting groups

Reporting group title	LF-PB 30 mg

Reporting group description:

LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Reporting group title	Placebo

Reporting group description:

Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Subject analysis set title	LF-PB 30 mg - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained.

Subject analysis set title	Placebo - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-treat (ITT) analysis set includes all randomized subjects who receive trial medication and from whom at least one measurement is obtained.

Subject analysis set title	LF-PB 30 mg - safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used to summarize the safety assessments.

Subject analysis set title	Placebo - safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety analysis set (SAF) includes all subjects who received 1 dose of LF-PB or placebo will be used to summarize the safety assessments.

Subject analysis set title	LF-PB 30 mg - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK population: The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic

Subject analysis set title	placebo - PK population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Pharmacokinetic (PK) analysis set includes all patients who have provided valid and interpretable PK assessments without protocol violation with a probable impact on the pharmacokinetic

Subject analysis set title	LF-PB 30 mg - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

Subject analysis set title	placebo - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) analysis set will include all subjects who complete the trial without any major deviations related to the assessment of the primary endpoint. Subject will be analysed according to treatment received.

Primary: Incidence of seromas requiring an aspiration by day 28 on ITT population

End point title	Incidence of seromas requiring an aspiration by day 28 on ITT population

End point description:

Incidence of seromas requiring aspiration by Day 28 was calculated as the percentage of subjects who underwent an aspiration of seromas (based on the investigator's evaluation of the echography at the operated axilla) between discharge or Visit 2 (Day 3) after surgery, and Visit 7 (Day 28). In case of two or more consecutive missing visits the worst-case scenario was assumed.

End point type	Primary

End point timeframe:

by Day 28

End point values	LF-PB 30 mg - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: percentage				
number (not applicable)				
yes	75.0	62.5		
no	25.0	37.5		

Statistical analyses

Statistical analysis title	LF-PB 30 mg vs placebo
Comparison groups	LF-PB 30 mg - ITT population v Placebo - ITT population
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.894 [1]
Method	Fisher exact
Parameter estimate	difference in incidence
Point estimate	12.5
Confidence interval	
level	95 %
sides	1-sided
upper limit	38.5

Notes:

[1] - One-sided Fisher’s exact test P-value

Primary: Incidence of seromas requiring an aspiration by day 28 on PP population

End point title	Incidence of seromas requiring an aspiration by day 28 on PP population

End point description:

Incidence of seromas requiring aspiration by Day 28 was calculated as the percentage of subjects who underwent an aspiration of seromas (based on the investigator’s evaluation of the echography at the operated axilla) between discharge or Visit 2 (Day 3) after surgery, and Visit 7 (Day 28). In case of two or more consecutive missing visits the worst-case scenario was assumed.

End point type	Primary

End point timeframe:

By day 28

End point values	LF-PB 30 mg - PP population	placebo - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	23		
Units: percentage				
number (not applicable)				
yes	78.3	65.2		
no	21.7	34.8		

Statistical analyses

Statistical analysis title	LF-PB 30 mg vs placebo
Comparison groups	LF-PB 30 mg - PP population v placebo - PP population
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.905
Method	Fisher exact
Parameter estimate	diffrence in incidence
Point estimate	13
Confidence interval	
level	95 %
sides	1-sided
upper limit	38.8

Secondary: Time to resolution of seroma

End point title	Time to resolution of seroma

End point description:

Seroma duration: seroma was considered resolved when at the corresponding visits no aspiration, based on the Investigator clinical evaluation, was required (the information was confirmed at the next visit or

at 7 days post ALND, whichever occurred first). If seroma was still present at the end of trial visit, the subject was censored. In case of recurrence of seroma (i.e. recurrence of seroma after the termination of previous one), the final duration was considered the cessation of last episode.

End point type	Secondary

End point timeframe:

At days 1, 3, 7, 11, 14, 21, 28, 56, 84

End point values	LF-PB 30 mg - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	15		
Units: days				
median (confidence interval 95%)	15.00 (3.0 to 23.0)	12.00 (3.00 to 19.00)		

Statistical analyses

Statistical analysis title	LF-PB 30 mg vs placebo
Comparison groups	LF-PB 30 mg - ITT population v Placebo - ITT population
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.534
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.79

Notes:

[2] - Hazard ratio, Confidence Interval and Likelihood Ratio test p-value are derived from Cox-proportional hazards regression model with Treatment as covariate variable

Secondary: Number of aspirations required

End point title	Number of aspirations required

End point description:

Number of aspirations when volume aspirate was more than zero. In case of recurrent seroma, the number of aspirations was cumulative.

End point type	Secondary

End point timeframe:

At days 3, 7, 11, 14, 21, 28, 56, 84

End point values	LF-PB 30 mg - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	15		
Units: number				
arithmetic mean (standard deviation)	3.6 (± 2.50)	4.1 (± 3.33)		

Statistical analyses

Statistical analysis title	LF-PB 30 mg vs placebo
Comparison groups	LF-PB 30 mg - ITT population v Placebo - ITT population
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.884
Method	Wilcoxon (Mann-Whitney)

Secondary: Total volume of fluid aspirated from seroma

End point title	Total volume of fluid aspirated from seroma

End point description:

Total Volume of Fluid aspirated from seroma after drain removal

End point type	Secondary

End point timeframe:

At days 1, 3, 7, 11, 14, 21, 28, 56, 84

End point values	LF-PB 30 mg - ITT population	Placebo - ITT population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	15		
Units: mL				
arithmetic mean (standard deviation)	461.1 (± 654.96)	445.0 (± 554.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax

End point title	Cmax

End point description:

PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4)

End point type	Secondary

End point timeframe:

Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28.

End point values	LF-PB 30 mg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: ng/mL				
arithmetic mean (standard deviation)	16.35 (± 8.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax

End point title	Tmax

End point description:

PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4)

End point type	Secondary

End point timeframe:

Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28.

End point values	LF-PB 30 mg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: hour				
arithmetic mean (standard deviation)	21.17 (± 25.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUClast

End point title	AUClast

End point description:

PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4)

End point type	Secondary

End point timeframe:

Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28.

End point values	LF-PB 30 mg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: hr*ng/mL				
arithmetic mean (standard deviation)	2229.28 (± 822.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: T1/2,z

End point title	T1/2,z

End point description:

PK samples will be collected pre-dose and 3, 6 and 24 hours post-dose. Samples will also be collected at each scheduled visit until 1 month post-surgery (through Visit 7 – Week 4)

End point type	Secondary

End point timeframe:

Day 0 (surgery), Days 1, 3, 7, 11, 14, 21, 28.

End point values	LF-PB 30 mg - PK population			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: hour				
arithmetic mean (standard deviation)	97.86 (± 64.23)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study, AE data will be obtained at all study visits, based on information spontaneously provided by the patient and/or through questioning

Adverse event reporting additional description:

An Adverse Event is "any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment". (ICH E2A)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	LF-PB 30 mg

Reporting group description:

LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. LF-PB was supplied as a vial of 10 plus 20 mg sterile freeze-dried octreotide acetate (active product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Reporting group title	Placebo

Reporting group description:

Placebo for LF-PB 30 mg was administered as a singular intramuscular (i.m.) injection. Placebo was supplied as a vial of 10 mg sterile freeze-dried soybean lecithin and 5 mg hydroxypropyl-beta-cyclodextrin (placebo product) and prefilled syringe of sterile reconstitution solvent (purified soybean lecithin, isopropyl myristate, and ethanol 96% v/v).

Serious adverse events	LF-PB 30 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	LF-PB 30 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 24 (58.33%)	14 / 24 (58.33%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm recurrence			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Dry gangrene			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Hot flush			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Hypertensive crisis			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 24 (16.67%)	4 / 24 (16.67%)	
occurrences (all)	4	7	
Injection site pain			
subjects affected / exposed	3 / 24 (12.50%)	2 / 24 (8.33%)	
occurrences (all)	3	2	
Pain			
subjects affected / exposed	3 / 24 (12.50%)	1 / 24 (4.17%)	
occurrences (all)	3	1	
Injection site erythema			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	2	
Injection site reaction			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	

Injection site urticaria			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast inflammation			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Eschar			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Wound complication			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Wound dehiscence			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	
occurrences (all)	1	1	

Leukopenia			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	5 / 24 (20.83%)	1 / 24 (4.17%)	
occurrences (all)	5	1	
Diarrhoea			
subjects affected / exposed	3 / 24 (12.50%)	1 / 24 (4.17%)	
occurrences (all)	3	1	
Nausea			
subjects affected / exposed	2 / 24 (8.33%)	2 / 24 (8.33%)	
occurrences (all)	2	2	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 24 (4.17%)	1 / 24 (4.17%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Rash erythematous			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 24 (0.00%)	2 / 24 (8.33%)	
occurrences (all)	0	2	
Infections and infestations			

Wound infection subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2	0 / 24 (0.00%) 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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No limitations or caveats are applicable to this summary of the results

Notes: