Clinical trial results:
A Prospective Study Evaluating the Safety and Effectiveness of EVARREST® Fibrin Sealant Patch in Controlling Mild or Moderate Hepatic Parenchyma or Soft Tissue Bleeding During Open Abdominal, Retroperitoneal, Pelvic and Thoracic (non-cardiac) Surgery in Pediatric Patients

Summary

EudraCT number	2019-004657-89
Trial protocol	GB
Global end of trial date	13 February 2025

Results information

Result version number	v1 (current)
This version publication date	14 February 2026
First version publication date	14 February 2026

Trial information

Trial identification

Sponsor protocol code	BIOS-16-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03255174
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ETHICON Inc.
Sponsor organisation address	1000 US Highway 202 S, Raritan, United States, NJ 08869
Public contact	Clinical Registry Group, ETHICON Inc., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, ETHICON Inc., ClinicalTrialsEU@its.jnj.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	13 February 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 February 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the safety and hemostatic effectiveness of EVARREST Fibrin Sealant Patch (EVARREST) in controlling mild or moderate soft tissue & parenchymal bleeding during open hepatic, abdominal, pelvic, retroperitoneal, and thoracic (non-cardiac) surgery in pediatric participants.

Protection of trial subjects:

The study was conducted in accordance with the Code of Federal Regulations, the UK statutory instruments, the International Council for Harmonization (ICH) Guideline for Good Clinical Practice (GCP), and the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2018
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	United States: 16
Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	35
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	12
Children (2-11 years)	18
Adolescents (12-17 years)	5
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 35 participants were treated in the study. All participants completed the study. This was a single-arm study.

Period 1

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

Arms

Arm title	EVARREST Fibrin Sealant Patch

Arm description:

Participants with mild or moderate soft tissue or parenchymal bleeding during open hepatic, abdominal, pelvic, retroperitoneal, and thoracic (non-cardiac) surgery were treated with EVARREST Fibrin Sealant Patch (EVARREST). EVARREST Fibrin Sealant Patch is a sterile, bio-absorbable combination product consisting of two constituent parts- a flexible matrix and a coating of biological components (human plasma-derived fibrinogen and thrombin) embedded in a flexible composite patch component used as an adjunct to hemostasis during surgery.

Arm type	Experimental
Investigational medicinal product name	EVARREST Fibrin Sealant Patch
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant
Routes of administration	Topical use

Dosage and administration details:

Participants with mild or moderate soft tissue or parenchymal bleeding were treated with EVARREST during surgical procedure.

Number of subjects in period 1	EVARREST Fibrin Sealant Patch
Started	35
Full analysis set	31 [1]
Completed	35

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Reported participants in the milestone are of full analysis set.

Baseline characteristics

Reporting groups	
Reporting group title	EVARREST Fibrin Sealant Patch

Reporting group description:

Participants with mild or moderate soft tissue or parenchymal bleeding during open hepatic, abdominal, pelvic, retroperitoneal, and thoracic (non-cardiac) surgery were treated with EVARREST Fibrin Sealant Patch (EVARREST). EVARREST Fibrin Sealant Patch is a sterile, bio-absorbable combination product consisting of two constituent parts- a flexible matrix and a coating of biological components (human plasma-derived fibrinogen and thrombin) embedded in a flexible composite patch component used as an adjunct to hemostasis during surgery.

Reporting group values	EVARREST Fibrin Sealant Patch	Total	
Number of subjects	35	35	
Age categorical Units: Subjects			
In Utero	0	0	
Preterm newborn infants (gestional age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days - 23 months)	12	12	
Children (2 - 11 years)	18	18	
12 - 17 years	5	5	
Adults (18 - 64 years)	0	0	
From 65 - 84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	4.59		
standard deviation	± 4.341	-	
Gender categorical Units: Subjects			
Male	20	20	
Female	15	15	

End points

End points reporting groups

Reporting group title	EVARREST Fibrin Sealant Patch

Reporting group description:

Participants with mild or moderate soft tissue or parenchymal bleeding during open hepatic, abdominal, pelvic, retroperitoneal, and thoracic (non-cardiac) surgery were treated with EVARREST Fibrin Sealant Patch (EVARREST). EVARREST Fibrin Sealant Patch is a sterile, bio-absorbable combination product consisting of two constituent parts- a flexible matrix and a coating of biological components (human plasma-derived fibrinogen and thrombin) embedded in a flexible composite patch component used as an adjunct to hemostasis during surgery.

Primary: Absolute Time to Hemostasis

End point title	Absolute Time to Hemostasis[1]

End point description:

Hemostasis was defined as no detectable bleeding at the Target Bleeding Site (TBS). Absolute time to hemostasis was defined as the absolute time elapsed from TBS identification to the last moment in time at which detectable bleeding at the TBS was observed. TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression.

End point type	Primary

End point timeframe:

During surgical procedure on Day 0 (from TBS identification to the last moment in time at which detectable bleeding at TBS observed)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: only descriptive data was planned to be reported for this endpoint.

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Minutes				
median (confidence interval 95%)	4.00 (4.00 to 4.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Hemostatic Success at 4 Minutes

End point title	Percentage of Participants who Achieved Hemostatic Success at 4 Minutes

End point description:

Percentage of participants who achieved hemostatic success at 4 minutes was reported. A participant was considered hemostatic success at 4 minutes if the TBS was hemostatic at 4 minutes, and there was no re-bleeding that required treatment (other than observation only) at the TBS from 4 minutes following the first TBS identification through final fascial closure. Hemostasis was assessed at 4 minutes

from TBS identification by carefully releasing manual compression and removing the surgical sponge (if used). TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression.

End point type	Secondary

End point timeframe:

4 minutes after TBS identification (during surgical procedure on Day 0)

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	77.4 (58.90 to 90.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events That Were Potentially Related to Bleeding at the TBS

End point title	Percentage of Participants with Adverse Events That Were Potentially Related to Bleeding at the TBS

End point description:

Percentage of participants with adverse events that were potentially related to bleeding at the TBS was reported. TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression. An adverse event means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An AE can be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a drug, without judgment about causality.

End point type	Secondary

End point timeframe:

From the day of surgical procedure (Day 0) up to 44-days post-surgery

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Percentage of participants				
number (not applicable)	5.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with No Re-bleeding at the TBS

End point title	Percentage of Participants with No Re-bleeding at the TBS

End point description:

Percentage of participants with no re-bleeding at the TBS was reported. TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression.

End point type	Secondary

End point timeframe:

During surgical procedure on Day 0 (from TBS identification to final fascial closure)

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Percentage of participants				
number (not applicable)	96.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Hemostatic Success at 10 Minutes

End point title	Percentage of Participants who Achieved Hemostatic Success at 10 Minutes

End point description:

Percentage of participants who achieved hemostatic success at 10 minutes was reported. A participant was considered hemostatic success at 10 minutes if the TBS was hemostatic at 10 minutes, and there was no re-bleeding that required treatment (other than observation only) at the TBS from 10 minutes following the first TBS identification through final fascial closure. Hemostasis was assessed at 10 minutes from TBS identification and at initiation of final fascial closure. TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression.

End point type	Secondary

End point timeframe:

10 minutes after TBS identification (during surgical procedure on Day 0)

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	93.5 (78.58 to 99.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events That Were Potentially Related to Thrombotic Events

End point title	Percentage of Participants with Adverse Events That Were Potentially Related to Thrombotic Events

End point description:

Percentage of participants with adverse events that were potentially related to thrombotic events at the TBS was reported. TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression. An adverse event means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An AE can be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a drug, without judgment about causality.

End point type	Secondary

End point timeframe:

From the day of surgical procedure (Day 0) up to 44-days post-surgery

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Re-treatment at the TBS

End point title	Percentage of Participants With Re-treatment at the TBS

End point description:

Percentage of participants with re-treatment at the TBS was reported. TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression.

End point type	Secondary

End point timeframe:

From the day of surgical procedure (Day 0) up to 44-days post-surgery

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Percentage of participants				
number (not applicable)	25.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events

End point description:

Percentage of participants with adverse events (including serious and non-serious) were reported. TBS was defined as the first accessible mild or moderate bleeding site identified in the hepatic parenchyma or soft tissue, where conventional methods of controlling bleeding were ineffective or impractical and was amenable to manual compression. An adverse event means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An AE can be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a drug, without judgment about causality.

End point type	Secondary

End point timeframe:

From the day of surgical procedure (Day 0) up to 44-days post-surgery

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Percentage of participants				
number (not applicable)	68.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Intraoperative Blood Loss

End point title	Estimated Intraoperative Blood Loss

End point description:

Estimated intraoperative blood loss was reported. Safety analysis set included all participants who received treatment. Here, 'N' (overall number of participants analyzed) signifies the number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

During surgical procedure on Day 0

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: Milliliters (mL)				
arithmetic mean (standard deviation)	81.9 (± 112.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Laboratory Parameter: Platelets

End point title	Change From Baseline in Laboratory Parameter: Platelets

End point description:

Change from baseline in laboratory parameter (platelets) was reported. Baseline was defined as the value that was the closest to the procedure time (the latest value). Safety analysis set included all participants who received treatment. Here, 'N' (overall number of participants analyzed) signifies the number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From baseline up to hospital discharge (up to 44-day post-surgery on Day 0)

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: 10^9 cells per liter				
arithmetic mean (standard deviation)	-18.87 (± 130.724)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Laboratory Parameter: Hematocrit

End point title	Change From Baseline in Laboratory Parameter: Hematocrit

End point description:

Change from baseline in laboratory parameter (hematocrit) was reported. Baseline was defined as the value that was the closest to the procedure time (the latest value). Safety analysis set included all participants who received treatment. Here, 'N' (overall number of participants analyzed) signifies the number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From baseline up to hospital discharge (up to 44-day post-surgery on Day 0)

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Liters per liter (L/L)				
arithmetic mean (standard deviation)	-0.02 (± 0.048)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Laboratory Parameter: Hemoglobin

End point title	Change From Baseline in Laboratory Parameter: Hemoglobin

End point description:

Change from baseline in laboratory parameter (hemoglobin) was reported. Baseline was defined as the value that was the closest to the procedure time (the latest value). Safety analysis set included all participants who received treatment. Here, 'N' (overall number of participants analyzed) signifies the number of participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From baseline up to hospital discharge (up to 44-day post-surgery on Day 0)

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)	-5.59 (± 16.353)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Blood Products Transfusion

End point title	Number of Participants With Blood Products Transfusion

End point description:

Number of participants with blood products transfused was reported. Safety analysis set included all participants who received treatment.

End point type	Secondary

End point timeframe:

From the day of surgical procedure (Day 0) up to 44-days post-surgery

End point values	EVARREST Fibrin Sealant Patch			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Participants	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the day of surgical procedure (Day 0) up to 44-days post-surgery	
Adverse event reporting additional description:	
Safety analysis set included all participants who received treatment.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	EVARREST Fibrin Sealant Patch
Reporting group description:	
Participants with mild or moderate soft tissue or parenchymal bleeding during open hepatic, abdominal, pelvic, retroperitoneal, and thoracic (non-cardiac) surgery were treated with EVARREST Fibrin Sealant Patch (EVARREST). EVARREST Fibrin Sealant Patch is a sterile, bio-absorbable combination product consisting of two constituent parts- a flexible matrix and a coating of biological components (human plasma-derived fibrinogen and thrombin) embedded in a flexible composite patch component used as an adjunct to hemostasis during surgery.	

Serious adverse events	EVARREST Fibrin Sealant Patch		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 35 (25.71%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Procedural vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Procedural pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural bile leak			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Central venous catheterisation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Respiratory syncytial virus infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			

alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Catheter site infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	EVARREST Fibrin Sealant Patch		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 35 (60.00%)		
Vascular disorders			
Hypotension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Hypertension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	11 / 35 (31.43%)		
occurrences (all)	15		
General disorders and administration site conditions			
Pyrexia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	9		
Peripheral swelling			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Impaired healing			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Feeling jittery			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Respiratory acidosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Bradypnoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Cough			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Dyspnoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Hypoxia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Rhinorrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Oropharyngeal pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Tachypnoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	4		
Psychiatric disorders			
Nervousness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Agitation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Product issues			
Device leakage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Blood lactic acid increased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Body temperature decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Blood magnesium abnormal				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Blood potassium decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	4 / 35 (11.43%)			
occurrences (all)	4			
Blood potassium abnormal				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Blood magnesium decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Coagulation time prolonged				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Body temperature increased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			

Culture urine positive				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Haemoglobin decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences (all)	2			
Hepatic enzyme increased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Liver function test abnormal				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Oxygen saturation decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	4 / 35 (11.43%)			
occurrences (all)	5			
Platelet count decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Prothrombin time abnormal				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences (all)	1			
Respiratory rate decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences (all)	2			
Staphylococcus test positive				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Weight decreased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Wound haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Procedural pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	11 / 35 (31.43%)		
occurrences (all)	11		
Procedural haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Procedural complication			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Incision site pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Cardiac disorders			
Bradycardia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Tachycardia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	10 / 35 (28.57%)		
occurrences (all)	13		
Nervous system disorders			
Tremor			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Somnolence			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Dyskinesia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Eye disorders			
Eye swelling			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Constipation			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	10 / 35 (28.57%)		
occurrences (all)	10		
Abdominal pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	5		
Abdominal distension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	4		
Vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	11		
Toothache			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Hepatobiliary disorders			
Retrograde portal vein flow			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Erythema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Rash			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	4		
Renal and urinary disorders			
Bladder dilatation			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Polyuria			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Muscle twitching			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Infections and infestations			
Clostridium difficile infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Enterobacter infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Influenza			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypokalaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Hypomagnesaemia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Hypophagia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2017	The overall rationale for the amendment-1 was to remove post-surgery lab tests.
05 February 2018	The overall rationale for the amendment-2 was to update the re-instate post-surgery lab tests per food and drug administration (FDA) request.
12 December 2019	The overall rationale for the amendment-3 was to addition of OUS (United Kingdom sites) – Not implemented in UK.
12 May 2020	The overall rationale for the amendment-4 was to update that 30-day follow-up (FU) visit could be by telephone (need for physical exam removed). The per protocol (PP) set should only exclude intent-to-treat (ITT) participants with major protocol deviations affecting the primary effectiveness endpoint, instead of all participants with major protocol deviations.
23 July 2021	The overall rationale for the amendment-5 was to exclude participants who received a coronavirus disease (COVID) vaccine within 4 weeks of surgery, or scheduled to have in follow-up period.
02 November 2023	The overall rationale for the amendment-6 was to remove age stratification (to allow participants less than [<] 1 year to be included at any stage of enrolment, not just final 4 participants).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported