Clinical trial results:
A Prospective, Randomized, Controlled Study Evaluating EVICEL® Fibrin Sealant as an Adjunct to Haemostasis During Abdominal, Retroperitoneal, Pelvic or Thoracic (Non-Cardiac) Surgery in Paediatric Patients

Summary

EudraCT number	2013-003401-26
Trial protocol	GB BE
Global end of trial date	17 May 2019

Results information

Result version number	v1 (current)
This version publication date	03 December 2019
First version publication date	03 December 2019

Trial information

Trial identification

Sponsor protocol code	400-12-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02227706
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ETHICON Inc
Sponsor organisation address	Route 22 West, Somerville, United States, 08876-0262
Public contact	Leonie Rynn, ETHICON Inc, 001 9082182492, lrynn1@its.jnj.com
Scientific contact	Leonie Rynn, ETHICON Inc, 001 9082182492, lrynn1@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001149-PIP01-11
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 May 2019
Global end of trial reached?	Yes
Global end of trial date	17 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and effectiveness of EVICEL® as an adjunct to achieve haemostasis during surgery in paediatric patients.

Protection of trial subjects:

Study information was presented to the patient and their legal guardian by a trained member of the research team. The final taking of informed consent was completed by the Investigator or sub−investigator when the potential participant and their legal guardian were completely satisfied with the information presented.

Venepuncture was required, however we minimised the number required and where possible results that were already available were used rather than repeating the test. All visits were conducted at times where the patient would routinely attend the hospital with the option to conduct the 30 day follow-up visit by telephone.

Physical examinations were undertaken by a trained member of the research team in a private area or room, or if this procedure was completed routinely upon admission to the hospital it was not repeated.

The study was reviewed and approved by the respective ethics committees in the countries where the study was being conducted.

Background therapy:

None.

Evidence for comparator:

With a clinical history spanning more than 50 years, SURGICEL® has been used as an adjunct to achieve and accelerate haemostasis when various types of bleeding were observed intra-operatively. The product can be placed on the source of bleeding with manual compression to facilitate haemostasis and was therefore considered a suitable control product for use in this study.

Actual start date of recruitment	05 November 2014
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	Canada: 4
Country: Number of subjects enrolled	United Kingdom: 36
Worldwide total number of subjects	40
EEA total number of subjects	36

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)	7
Children (2-11 years)	13
Adolescents (12-17 years)	20
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first subject was recruited on 5th November 2014 and the last subject was recruited on 17th April 2019. The last subject's last visit took place on 17th May 2019.

Pre-assignment

Screening details:

Prospective subjects were screened within 21 days prior to surgery. Prior to any study related procedures, subjects and/or parent or legal representative were fully informed of all aspects of the study. Subjects and/or their parent or legal representative were asked to sign a Consent Form or assent, as applicable.

Period 1

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

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	EVICEL®

Arm description:

EVICEL® is a human plasma derived fibrin sealant consisting of two components: (1) Biologically Active Component 2 (BAC2), a concentrate of human clottable protein (containing mainly human fibrinogen and fribrinectin), and (2) human thrombin.

Arm type	Experimental
Investigational medicinal product name	EVICEL®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for sealant
Routes of administration	Epilesional use

Dosage and administration details:

For each subject, at least one EVICEL® (BAC2 and Thrombin) kit was thawed and available for administration prior to randomization. EVICEL® was to be sprayed or dripped onto the tissue to produce a thin, even layer.

Arm title	SURGICEL®

Arm description:

SURGICEL® Absorbable hemostat is a sterile absorbable knitted fabric prepared by controlled oxidation of regenerated cellulose.

Arm type	Active comparator
Investigational medicinal product name	SURGICEL® Original
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sealant matrix
Routes of administration	Topical use

Dosage and administration details:

For subjects randomized to SURGICEL®, the product was to be applied and held firmly on the TBS, immediately after randomization according to the product instructions for use.

Number of subjects in period 1	EVICEL®	SURGICEL®
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups	
Reporting group title	EVICEL®
Reporting group description:	
EVICEL® is a human plasma derived fibrin sealant consisting of two components: (1) Biologically Active Component 2 (BAC2), a concentrate of human clottable protein (containing mainly human fibrinogen and fribrinectin), and (2) human thrombin.	
Reporting group title	SURGICEL®
Reporting group description:	
SURGICEL® Absorbable hemostat is a sterile absorbable knitted fabric prepared by controlled oxidation of regenerated cellulose.	

Reporting group values	EVICEL®	SURGICEL®	Total
Number of subjects	20	20	40
Age Categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	5	2	7
Children (2-11 years)	4	9	13
Adolescents (12-17 years)	11	9	20
Age Continuous			
Units: years			
arithmetic mean	9.4	9.0	
full range (min-max)	0.9 to 17.0	1.0 to 17.0	-
Gender Categorical			
Units: Subjects			
Female	11	7	18
Male	9	13	22

Subject analysis sets	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised subjects	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
Full analysis set who had no major protocol deviations	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who received treatment	

Reporting group values	Full Analysis Set	Per Protocol	Safety Set
Number of subjects	40	38	40
Age Categorical			
Units: Subjects			

Infants and toddlers (28 days-23 months)	7	7	7
Children (2-11 years)	13	13	13
Adolescents (12-17 years)	20	18	20
Age Continuous			
Units: years			
arithmetic mean	9.2	8.9	9.2
full range (min-max)	0.9 to 17.0	0.9 to 17.0	0.9 to 17.0
Gender Categorical			
Units: Subjects			
Female	18	18	18
Male	22	20	22

End points

End points reporting groups

Reporting group title	EVICEL®
Reporting group description:	
EVICEL® is a human plasma derived fibrin sealant consisting of two components: (1) Biologically Active Component 2 (BAC2), a concentrate of human clottable protein (containing mainly human fibrinogen and fribrinectin), and (2) human thrombin.	
Reporting group title	SURGICEL®
Reporting group description:	
SURGICEL® Absorbable hemostat is a sterile absorbable knitted fabric prepared by controlled oxidation of regenerated cellulose.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised subjects	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
Full analysis set who had no major protocol deviations	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who received treatment	

Primary: Absolute Time to Haemostasis

End point title	Absolute Time to Haemostasis[1]
End point description:	
Absolute time to haemostasis, defined as absolute time when there was no detectable bleeding at the Target Bleeding Site (TBS)	
End point type	Primary
End point timeframe:	
From randomisation	

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: The primary effectiveness endpoint is summarized descriptively by treatment group.

End point values	EVICEL®	SURGICEL®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Minutes				
median (confidence interval 95%)				
Absolute time to haemostasis	4.0 (3.3 to 4.7)	4.0 (2.9 to 8.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Haemostasis at Target Bleeding Site at 4 Minutes

End point title	Haemostasis at Target Bleeding Site at 4 Minutes

End point description:

Haemostasis at 4 Minutes

End point type	Secondary

End point timeframe:

Intra-operatively from randomisation to 4 minutes after randomisation

End point values	EVICEL®	SURGICEL®	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20	20	40	
Units: Subject				
Haemostasis at 4 Minutes	16	13	29	

Statistical analyses

No statistical analyses for this end point

Secondary: Haemostasis at Target Bleeding Site at 7 Minutes

End point title	Haemostasis at Target Bleeding Site at 7 Minutes

End point description:

Haemostasis at 7 Minutes

End point type	Secondary

End point timeframe:

Intra-operatively from randomisation to 7 minutes after randomisation

End point values	EVICEL®	SURGICEL®	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20	20	40	
Units: Subject				
Haemostasis at 7 Minutes	20	16	36	

Statistical analyses

No statistical analyses for this end point

Secondary: Haemostasis at Target Bleeding Site at 10 Minutes

End point title	Haemostasis at Target Bleeding Site at 10 Minutes

End point description:

Haemostasis at 10 Minutes

End point type	Secondary

End point timeframe:

Intra-operatively from randomisation to 10 minutes after randomisation

End point values	EVICEL®	SURGICEL®	Full Analysis Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	20	20	40	
Units: Subject				
Haemostasis at 10 Minutes	19	18	37	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Treatment Failures

End point title	Incidence of Treatment Failures

End point description:

Defined as haemostasis not achieved within 10 minutes or bleeding requiring treatment other than re-application of the assigned haemostatic adjunct within 10 minutes.

End point type	Secondary

End point timeframe:

10 minutes

End point values	EVICEL®	SURGICEL®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Number of subjects (failure)	1	5		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects with a Thrombotic Event

End point title	Number of Subjects with a Thrombotic Event

End point description:

End point type	Other pre-specified

End point timeframe:

From randomisation up to 30 days (+/- 14 days) following surgery

End point values	EVICEL®	SURGICEL®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Subjects				
Number of subjects with thrombotic events	0	0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Subjects with an Adverse Event Related to Re-bleeding at Target Bleeding Site

End point title	Number of Subjects with an Adverse Event Related to Re-bleeding at Target Bleeding Site

End point description:

End point type	Other pre-specified

End point timeframe:

From randomisation to 30 days (+/- 14 days) following surgery

End point values	EVICEL®	SURGICEL®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Subject				
Subjects with AE related to re-bleeding at TBS	1	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from point of randomisation, during the procedure, throughout hospital admission and until completion of the 30 day (+/-14 day) follow up visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	EVICEL®

Reporting group description:

EVICEL® is a human plasma derived fibrin sealant consisting of two components: (1) Biologically Active Component 2 (BAC2), a concentrate of human clottable protein (containing mainly human fibrinogen and fribrinectin), and (2) human thrombin.

Reporting group title	SURGICEL®

Reporting group description:

SURGICEL® Absorbable hemostat is a sterile absorbable knitted fabric prepared by controlled oxidation of regenerated cellulose.

Serious adverse events	EVICEL®	SURGICEL®	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 20 (20.00%)	3 / 20 (15.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Castleman's disease			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Procedural complication			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Ureteral stent removal			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain Injury	Additional description: Hypoxic Brain Injury		
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Varicella	Additional description: Chicken Pox		
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EVICEL®	SURGICEL®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 20 (90.00%)	20 / 20 (100.00%)	
Vascular disorders			

Haemorrhage			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Hypertension			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Hypotension			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	3	
Surgical and medical procedures			
Wound drainage			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Device occlusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	8 / 20 (40.00%)	6 / 20 (30.00%)	
occurrences (all)	9	7	
Swelling			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Atelectasis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Cough			
subjects affected / exposed	1 / 20 (5.00%)	3 / 20 (15.00%)	
occurrences (all)	1	3	
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Haemoptysis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hyperventilation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Neonatal aspiration			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pneumothorax			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Respiratory depression			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tachypnoea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Investigations			

Blood potassium decreased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Haemoglobin decreased			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Oxygen saturation decreased			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	3	
Respiratory rate decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Respiratory rate increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Urine output decreased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
White blood cell count increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Procedural complication			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	7 / 20 (35.00%)	5 / 20 (25.00%)	
occurrences (all)	8	5	
Wound complication			

subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Wound secretion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Tachycardia			
subjects affected / exposed	3 / 20 (15.00%)	6 / 20 (30.00%)	
occurrences (all)	3	6	
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Febrile neutropenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	5 / 20 (25.00%)	3 / 20 (15.00%)	
occurrences (all)	5	3	
Abdominal pain lower			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)	4 / 20 (20.00%)	
occurrences (all)	3	4	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Ileus			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Mucous stools			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	2	
Teething			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	

Vomiting			
subjects affected / exposed	3 / 20 (15.00%)	6 / 20 (30.00%)	
occurrences (all)	3	6	
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Decubitus ulcer			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dermatitis diaper			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Livedo reticularis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Rash			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Rash erythematous			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Polyuria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

Musculoskeletal pain			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Infections and infestations			
Candidiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Orchitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Post procedural infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Viral infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Wound infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Fluid overload			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hyponatraemic syndrome			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	1 / 20 (5.00%)	3 / 20 (15.00%)	
occurrences (all)	1	3	
Metabolic acidosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Polydipsia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 October 2013	A number of up-dates were made including the following - Product application technique, product labeling and shipping; visit timelines; primary and secondary endpoint clarifications to align with the Paediatric Investigation Plan (PIP); up-dates to the description of the analysis for success/failure data; administrative up-dates
31 July 2015	A number of up-dates were made including the following - Addition of parenchymal organ bleeding; up-date to the definition of open procedure and infected field; airless spray accessory device added; administrative up-dates
29 February 2016	A number of up-dates were made including the following - Up-dated to reflect the change in age group specifications for study recruitment; up-dated to further define treatment failure; clarification on statistical analysis for primary and secondary endpoints, laboratory values and handling of missing data; administrative up-dates
08 January 2018	A number of up-dates were made including the following - Removal of age stratification; further clarification on open procedure definition; additional information on product storage conditions; product application clarifications; administrative up-dates

Notes:

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.

Two subjects in the control arm were haemostatic at the TBS at 10 minutes however they subsequently rebled requiring additional treatment and were conservatively considered a failure for the secondary endpoint of Incidence of Treatment Failures.

Notes: