Clinical trial results:
A Prospective, Randomised, Active-Controlled, Single-blind, Parallel Group Clinical Trial to Evaluate the Safety and Efficacy of Fibrin Sealant Grifols (FS Grifols) as an Adjunct to Haemostasis during Surgery in Paediatric Subjects.

Summary

EudraCT number	2016-004489-24
Trial protocol	BG HU DE FR SE GB RO
Global end of trial date	20 May 2022

Results information

Result version number	v2 (current)
This version publication date	23 June 2023
First version publication date	15 December 2022
Version creation reason	• Correction of full data set Minor changes required

Trial information

Trial identification

Sponsor protocol code	IG1405

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03461406
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Instituto Grifols, S.A
Sponsor organisation address	Can Guasch, 2, Parets del Vallès, Barcelona, Spain, 08150
Public contact	Department of Drug Development, Instituto Grifols, S.A., 34 935712000, IGregulatory.affairs@grifols.com
Scientific contact	Department of Drug Development, Instituto Grifols, S.A., 34 935712000, IGregulatory.affairs@grifols.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001598-PIP01-13
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	20 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study is to evaluate if FS Grifols is non-inferior to EVICEL® in terms of the percentage of subjects achieving hemostasis at the target bleeding site (TBS) by 4 minutes (T4) from the start of treatment application (TStart) with no occurrence of rebleeding until the completion of the surgical closure by layers of the exposed surgical field containing the TBS (TClosure).

Protection of trial subjects:

Written Informed Consent Form (ICF) by the subject or a parent and/or legal guardian along with subject assent were obtained before any study specific procedure took place.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 28
Country: Number of subjects enrolled	Bulgaria: 26
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 21
Country: Number of subjects enrolled	Romania: 62
Country: Number of subjects enrolled	Serbia: 44
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	186
EEA total number of subjects	110

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	6
Infants and toddlers (28 days-23 months)	37

Children (2-11 years)	67
Adolescents (12-17 years)	76
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at sites in the United States, Bulgaria, France, Hungary, Romania, Serbia, and United Kingdom, from 18 January 2019 (first subject enrolled to receive the study drug) to 20 May 2022 (last subject completed).

Pre-assignment

Screening details:

Paediatric subjects with excessive bleeding during surgery were randomized into 1: 1 ratio to receive FS Grifols and EVICEL. A total of 197 subjects were screened, out of which 186 subjects were randomized (Intent-to-treat population), 178 received study treatment (modified intent-to-treat population), 171 subjects completed the study.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Fibrin Sealant Grifols

Arm description:

Subjects topically applied FS Grifols, which consisted of component 1: human fibrinogen (80 mg/mL) and component 2: human thrombin with calcium chloride (500 IU/mL) solutions filled in syringes and assembled on a syringe holder.

Arm type	Experimental
Investigational medicinal product name	FS Grifols
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal spray, solution
Routes of administration	Topical

Dosage and administration details:

The FE Grifols solution was applied topically via drip or spray application.

Arm title	EVICEL

Arm description:

Subjects topically applied EVICEL, which consisted of component 1: Concentrate of human fibrinogen (BAC 2) (55-85 mg/mL) and component 2: human thrombin (800-1200 IU/mL) solutions. The 2 components (BAC2 and thrombin) were mixed and applied topically.

Arm type	Active comparator
Investigational medicinal product name	EVICEL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal spray, solution
Routes of administration	Topical

Dosage and administration details:

The EVICEL solution was applied topically via drip or spray application.

Number of subjects in period 1	Fibrin Sealant Grifols	EVICEL
Started	95	91
Parenchymous Surgery	46	43
Soft Tissue Surgery	45	44
Safety Population	91	87
Completed	87	84
Not completed	8	7
Consent withdrawn by subject	-	1
Death	1	2
Screen failure	3	1
Lost to follow-up	3	-
Reason not specified	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Fibrin Sealant Grifols
Reporting group description:	
Subjects topically applied FS Grifols, which consisted of component 1: human fibrinogen (80 mg/mL) and component 2: human thrombin with calcium chloride (500 IU/mL) solutions filled in syringes and assembled on a syringe holder.	
Reporting group title	EVICEL
Reporting group description:	
Subjects topically applied EVICEL, which consisted of component 1: Concentrate of human fibrinogen (BAC 2) (55-85 mg/mL) and component 2: human thrombin (800-1200 IU/mL) solutions. The 2 components (BAC2 and thrombin) were mixed and applied topically.	

Reporting group values	Fibrin Sealant Grifols	EVICEL	Total
Number of subjects	95	91	186
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 8.43 ± 6.108	 8.84 ± 6.320	 -
Gender categorical Units: Subjects			
Female	40	30	70
Male	55	61	116

End points

End points reporting groups

Reporting group title	Fibrin Sealant Grifols
Reporting group description:	
Subjects topically applied FS Grifols, which consisted of component 1: human fibrinogen (80 mg/mL) and component 2: human thrombin with calcium chloride (500 IU/mL) solutions filled in syringes and assembled on a syringe holder.	
Reporting group title	EVICEL
Reporting group description:	
Subjects topically applied EVICEL, which consisted of component 1: Concentrate of human fibrinogen (BAC 2) (55-85 mg/mL) and component 2: human thrombin (800-1200 IU/mL) solutions. The 2 components (BAC2 and thrombin) were mixed and applied topically.	

Primary: Percentage of Subjects Achieving Hemostasis Within 4 Minutes After Treatment Start (T4)

End point title	Percentage of Subjects Achieving Hemostasis Within 4 Minutes After Treatment Start (T4)
End point description:	
Hemostasis is defined as Grade 0 bleeding per 5-point validated bleeding severity scale (0=no bleeding and 4=Unidentified or inaccessible spurting or gush) at the target bleeding site (TBS) according to the investigator's (surgeon's) judgment, so that the surgical closure of the exposed field could begin. Modified ITT (mITT) population included all subjects in the ITT population who meet the intra-operative enrollment criteria, and thus treated with any amount of investigational product (IP). Overall number analysed are the number of participants with haemostasis by 4 minutes. 'n' indicates the number of participants with parenchymous and soft tissue surgery with data available for analysis. Percentage are rounded off the single decimal point.	
End point type	Primary
End point timeframe:	
From start of treatment until 4 minutes after treatment start (Day 1)	

End point values	Fibrin Sealant Grifols	EVICEL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	87		
Units: percentage of subjects				
number (not applicable)				
Parenchymous Surgery (n=46, 43)	100.0	100.0		
Soft Tissue Surgery (n=45,44)	93.3	90.9		

Statistical analyses

Statistical analysis title	Hemostasis by 4 Minutes (Parenchymous)
Comparison groups	Fibrin Sealant Grifols v EVICEL

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.09

Statistical analysis title	Hemostasis by 4 Minutes (Soft Tissue)
Comparison groups	Fibrin Sealant Grifols v EVICEL
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.16

Secondary: Cumulative Percentage of Subjects Achieving Hemostasis at the TBS by the 7 Minutes After Treatment Start (T7)

End point title	Cumulative Percentage of Subjects Achieving Hemostasis at the TBS by the 7 Minutes After Treatment Start (T7)

End point description:

Hemostasis = Grade 0 bleeding per 5-point validated bleeding severity scale (0=no bleeding and 4=Unidentified or inaccessible spurting or gush) at the TBS according to the investigator’s (surgeon’s) judgment, so that surgical closure of the exposed field could begin. Cumulative percentage of subjects achieving hemostasis at the TBS by time points of T7 defined as an absence/cessation of bleeding (Grade 0) at the TBS by that time point without occurrence of rebleeding, Grade 3 or Grade 4 bleeding, use of alternative hemostatic treatment, and reapplication of study treatment after T4 and until TClosure. mITT population=all subjects in ITT population who meet intra-operative enrollment criteria, and thus treated with any amount of investigational product (IP). Overall number analysed are number of participants with haemostasis by 7 minutes. 'n' = number of participants with parenchymous and soft tissue surgery with data for analysis. Percentages are rounded off a single decimal point.

End point type	Secondary

End point timeframe:

From start of treatment to 7 minutes after start of treatment (Day 1)

End point values	Fibrin Sealant Grifols	EVICEL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	87		
Units: percentage of subjects				
number (not applicable)				
Parenchymous Surgery (n=46,43)	100.0	100.0		
Soft Tissue Surgery (n=45,44)	100.0	100.0		

Statistical analyses

Statistical analysis title	Hemostasis by 7 Minutes (Parenchymous)
Comparison groups	Fibrin Sealant Grifols v EVICEL
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.09

Statistical analysis title	Hemostasis by 7 Minutes (Soft tissue)
Comparison groups	Fibrin Sealant Grifols v EVICEL
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.09

Secondary: Cumulative Percentage of Subjects Achieving Hemostasis at the Target Bleeding Site by 10 Minutes After Treatment Start (T10)

End point title	Cumulative Percentage of Subjects Achieving Hemostasis at the Target Bleeding Site by 10 Minutes After Treatment Start (T10)

End point description:

Hemostasis is defined as Grade 0 bleeding at the TBS according to the investigator's (surgeon's) judgment, so that the surgical closure of the exposed field could begin. The cumulative percentage of subjects achieving hemostasis at the TBS by the time points of T10 defined as an absence/cessation of bleeding (Grade 0) at the TBS by that time point without occurrence of rebleeding, Grade 3 or Grade 4 bleeding, use of alternative hemostatic treatment, and reapplication of study treatment after T4 and until TClosure. mITT population included all participants in the ITT population who meet the intra-operative enrollment criteria and thus treated with any amount of IP. Overall number analyzed are the number of participants with haemostasis by 10 minutes. 'n' indicates number analyzed are the number of participants with parenchymous and soft tissue surgery with data available for analysis. Percentages are rounded off the single decimal point.

End point type	Secondary

End point timeframe:

From start of treatment to 10 minutes after start of treatment (Day 1)

End point values	Fibrin Sealant Grifols	EVICEL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	87		
Units: percentage of subjects				
number (not applicable)				
Parenchymous Surgery (n=45,43)	97.8	100.0		
Soft Tissue Surgery (n=45,44)	100.0	100.0		

Statistical analyses

Statistical analysis title	Hemostasis by 10 Minutes (Parenchymous)
Comparison groups	Fibrin Sealant Grifols v EVICEL
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.02

Statistical analysis title	Hemostasis by 10 Minutes (Soft tissue)
Comparison groups	Fibrin Sealant Grifols v EVICEL

Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Relative risk
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.09

Secondary: Percentage of Participants With Treatment Failures

End point title	Percentage of Participants With Treatment Failures

End point description:

Subjects were considered treatment failures if there is persistent bleeding at TBS beyond T4. Grade 3/Grade 4 breakthrough bleeding from TBS that jeopardizes subject safety according to investigator's judgment at any moment during 10-minute observational period and until TClosure. Use of alternative hemostatic treatments or maneuvers(other than study treatment) at TBS during 10-minute observational period and until TClosure, or use of study treatment at TBS beyond T4 and until TClosure. Rebleeding (Grade ≥1) at TBS after assessment of primary efficacy endpoint at T4 and until TClosure. mITT population: all participants in ITT population who meet intra-operative enrollment criteria and thus treated with any amount of IP. Overall number analyzed are number of participants with haemostasis by 4 minutes. 'n' indicates number of participants with parenchymous and soft tissue surgery with data available for analysis. Percentages are rounded off a single decimal point.

End point type	Secondary

End point timeframe:

From start of treatment up to 10 minutes after start of treatment and until the time of completion of surgical closure (Day 1)

End point values	Fibrin Sealant Grifols	EVICEL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	87		
Units: Subjects				
Parenchymous Surgery (n=46,43)	0	0		
Soft Tissue Surgery (n=45,44)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From signing informed consent form through the final study visit (30 ± 7 days post operative)	
Adverse event reporting additional description:	
The Safety population included all subjects who receive any amount of IP	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	EVICEL
Reporting group description:	
Subjects received EVICEL, which consists of component 1: Concentrate of human fibrinogen (BAC 2) (55-85 mg/mL) and component 2: human thrombin human thrombin (800-1200 IU/mL) solutions. The 2 components (BAC2 and thrombin) were mixed and applied topically.	
Reporting group title	Fibrin Sealant Grifols
Reporting group description:	
Subjects received FS Grifols, which consists of component 1: human fibrinogen (80 mg/mL) and component 2: human thrombin with calcium chloride (500 IU/mL) solutions filled in syringes and assembled on a syringe holder.	

Serious adverse events	EVICEL	Fibrin Sealant Grifols	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 87 (10.34%)	8 / 91 (8.79%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	2	1	
Investigations			
Transaminases increased			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
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			
Post procedural haemorrhage			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			

subjects affected / exposed	1 / 87 (1.15%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 87 (0.00%)	2 / 91 (2.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			

subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (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			
Postoperative wound infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory tract infection			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EVICEL	Fibrin Sealant Grifols	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 87 (14.94%)	20 / 91 (21.98%)	
Investigations			
Blood magnesium decreased			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Haemoglobin decreased			
subjects affected / exposed	1 / 87 (1.15%)	1 / 91 (1.10%)	
occurrences (all)	1	1	
Oxygen saturation decreased			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Platelet count increased			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	

Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Mechanical ventilation complication			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Procedural vomiting			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Wound complication			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Wound dehiscence			
subjects affected / exposed	0 / 87 (0.00%)	2 / 91 (2.20%)	
occurrences (all)	0	2	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 87 (0.00%)	2 / 91 (2.20%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 87 (3.45%)	2 / 91 (2.20%)	
occurrences (all)	3	2	
General disorders and administration site conditions			
Generalised oedema			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	5 / 87 (5.75%)	0 / 91 (0.00%)	
occurrences (all)	6	0	
Gastrointestinal disorders			

Abdominal distension			
subjects affected / exposed	0 / 87 (0.00%)	2 / 91 (2.20%)	
occurrences (all)	0	2	
Abdominal pain			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Intra-abdominal fluid collection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Melaena			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	2 / 87 (2.30%)	1 / 91 (1.10%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	3 / 87 (3.45%)	5 / 91 (5.49%)	
occurrences (all)	3	5	
Reproductive system and breast disorders			
Acquired hydrocele			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Bronchospasm			
subjects affected / exposed	1 / 87 (1.15%)	1 / 91 (1.10%)	
occurrences (all)	1	1	
Cough			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Epistaxis			

subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Pneumothorax			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Postoperative abscess			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Wound infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	0 / 87 (0.00%)	1 / 91 (1.10%)	
occurrences (all)	0	1	
Hypoalbuminaemia			

subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 91 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 May 2019	The purpose of the amendment was to revise to describe the modifications made to the FS Grifols container and packaging and revise to describe the modified procedure for the spray application because the original applicator was replaced. The new applicator is a Dual Applicator tip, which does not require gas pressure and can be used for both drip and spray applications of the IP.
06 November 2019	The purpose of the amendment was to update the number of subjects allowed to enroll into the study. To update to clarify that subjects participating or planning to participate in any other study will not be allowed to enroll in this study. To revise to clarify the amount of IP allowed for each age group and to correct the recommended psi for EVICEL application.
02 November 2021	The purpose of the amendment was to update to allow enrollment of preterm (up to gestational age <37 week) and term newborn infants (0 to 27 days) undergoing emergency (non-elective) surgery, per FDA advice. To revise to allow for flexibility in enrollment if hepatic surgeries are less than 50%. To update number of subjects planned in case of under or over enrollment. To update to further define and clarify the demographic information to be recorded and to clarify all Screening and to updated to describe FDA regulations and guidance for recording race information.
11 November 2021	The purpose of the amendment was a administrative change to remove incorrect headers.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported