Clinical trial results:
A prospective, open, randomized, academic phase II, two-arm trial evaluating the effect of fibrin-coated collagen (TachoSil®) on postoperative pancreatic leakage and fistula formation from the pancreato-enteric anastomosis in patients undergoing partial pancreaticoduodenectomy

Summary

EudraCT number	2013-000639-29
Trial protocol	AT
Global end of trial date	20 February 2017

Results information

Result version number	v1 (current)
This version publication date	26 August 2021
First version publication date	26 August 2021

Trial information

Trial identification

Sponsor protocol code	ABCSG_P00

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ABCSG (Austrian Breast & Colorectal Cancer Study Group)
Sponsor organisation address	Nußdorfer Platz 8/12, Vienna, Austria, 1190
Public contact	Hannes Fohler (Trial Office Director), ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsg.at
Scientific contact	Prof. Martin Schindl, ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsg.at

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	22 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 March 2015
Global end of trial reached?	Yes
Global end of trial date	20 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that fibrin-coated collagen patch (TachoSil) significantly decreases postoperative pancreatic leakage and prevents pancreatic fistula formation in patients undergoing partial pancreatico-duodenectomy with pancreato-enteric anastomosis.

Protection of trial subjects:

A Data Monitoring Committee (DMC) was established to obtain patient safety. The responsibility of the DMC was to evaluate deviations of medical relevance and safety issues. The DMC decided whether or not the patient should continue the study treatment due to safety issues. Important protocol deviations (IPDs) include all deviations endangering the basal medical concept of the study jeopardizing the safety of the patient. Other protocol deviations (PDs) include all other protocol deviations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 September 2013
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	Austria: 142
Worldwide total number of subjects	142
EEA total number of subjects	142

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)	55
From 65 to 84 years	86

85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study consisted of a planned recruitment phase of 36 months, the actual recruitment was completed in a shorter time frame (Sep 2013 - Feb 2015).

Pre-assignment

Screening details:

Eligibility had to be assessed max 14 days prior to surgery.

Pre-assignment period milestones

Number of subjects started	142
Number of subjects completed	142

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Tachosil

Arm description:

TachoSil® 9.5 cm x 4.8 cm (Non Investigational Medicinal Product, NIMP); Arm A (treatment arm): pancreato-jejunostomy was sealed with two patches of Tachosil® that were placed onto the anterior and posterior aspect of the anastomosis according to the manufacturer's user guide thereby wrapping it up entirely with a 2 cm rim on both the jejunal wall and the pancreatic tissue, respectively.

Arm type	NIMP intra-operative treatment
Investigational medicinal product name	TachoSil
Investigational medicinal product code	B02BC30
Other name	
Pharmaceutical forms	Medicated sponge
Routes of administration	Local use

Dosage and administration details:

2 patches (9,5cm x 4,8cm) during the surgery

Arm title	No Tachosil

Arm description:

Arm B (control arm): pancreatico-jejunostomy was left without any sealant.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Tachosil	No Tachosil
Started	71	71
Completed	64	58
Not completed	7	13
Adverse event, serious fatal	1	4
Consent withdrawn by subject	1	-
Lost to follow-up	5	9

Baseline characteristics

Reporting groups	
Reporting group title	Tachosil
Reporting group description:	
TachoSil® 9.5 cm x 4.8 cm (Non Investigational Medicinal Product, NIMP); Arm A (treatment arm): pancreato-jejunostomy was sealed with two patches of Tachosil® that were placed onto the anterior and posterior aspect of the anastomosis according to the manufacturer's user guide thereby wrapping it up entirely with a 2 cm rim on both the jejunal wall and the pancreatic tissue, respectively.	
Reporting group title	No Tachosil
Reporting group description:	
Arm B (control arm): pancreatico-jejunostomy was left without any sealant.	

Reporting group values	Tachosil	No Tachosil	Total
Number of subjects	71	71	142
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	29	26	55
From 65-84 years	42	44	86
85 years and over	0	1	1
Age continuous Units: years			
median	66	68	
full range (min-max)	48 to 83	39 to 86	-
Gender categorical Units: Subjects			
Female	37	38	75
Male	34	33	67
Body Mass Index (BMI)			
in kg/m²			
Units: Subjects			
<30	57	60	117
>=30	14	8	22
Missing	0	3	3
Neoadjuvant therapy Units: Subjects			
Yes	3	3	6
No	68	68	136
Pancreatic duct size			
in mm			
Units: Subjects			
<=4	50	47	97

>4	21	24	45
Pancreatic gland texture Units: Subjects			
Soft	42	35	77
Normal-firm	29	34	63
Missing	0	2	2

End points

End points reporting groups

Reporting group title	Tachosil

Reporting group description:

TachoSil® 9.5 cm x 4.8 cm (Non Investigational Medicinal Product, NIMP); Arm A (treatment arm): pancreato-jejunostomy was sealed with two patches of Tachosil® that were placed onto the anterior and posterior aspect of the anastomosis according to the manufacturer's user guide thereby wrapping it up entirely with a 2 cm rim on both the jejunal wall and the pancreatic tissue, respectively.

Reporting group title	No Tachosil

Reporting group description:

Arm B (control arm): pancreatico-jejunostomy was left without any sealant.

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

Subject analysis set description:

The primary analysis was based upon the ITT population, which consisted of all randomized patients with signed informed consent. Every patient was analyzed according to the randomized treatment group. Secondary endpoint analyses were based on all randomized patients with one exception: for the analysis of pancreatic fistula formation grading patients who underwent other types of surgery than PDPJ were not considered.

Primary: Leakage/Fistula

End point title	Leakage/Fistula

End point description:

Primary endpoint of the study was the evidence of pancreatic leakage or fistula according to International Study Group on Pancreatic Fistula Definition (ISGPF) definition. The definition of pancreatic fistula by the International Study Group on Pancreatic Fistula Definition (ISGPF), defining a pancreatic leak / fistula as fluid drainage rich in amylase > 3x serum amylase concentration on or after the 3rd postoperative day by an operative or interventional placed drainage was used to determine pancreatic leakage on a daily basis. Drains were removed, if the concentration of enzymes in the drain fluid was less 3x serum concentration for 2 consecutive days. If the enzyme concentration was above this limit, by definition a pancreatic leak / fistula was present and drains had to stay in place either until enzyme concentration was below this limit or the drain volume was less than 50 ml/day. If this was the case, drains were retracted stepwise until complete removal.

End point type	Primary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Subjects				
fistula	45	40		
no fistula	26	31		

Statistical analyses

Statistical analysis title	Primary endpoint analysis

Statistical analysis description:

The proportions of patients with leakage/fistula between the experimental and the control group were compared using a Chi-squared test or Fisher’s exact test depending on the underlying distribution. The effect of TachoSil® was considered meaningful if the proportion of patients with leakage/fistula was significantly lower in the experimental group compared to the control group.

Comparison groups	Tachosil v No Tachosil
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.392
Method	Chi-squared

Notes:

[1] - The null hypothesis (H0) of this study states that the proportion of patients with pancreatic leakage and fistula rates are the same between treatment group and control group. The alternative hypothesis (H1) states that the proportion of patients with pancreatic leakage and fistula rates are different between treatment group and control group.

Secondary: Leakage/Fistula - grading

End point title	Leakage/Fistula - grading

End point description:

One secondary endpoint was the evidence of any conditions / complications in association with pancreatic fistula formation measured according to the clinical severity grading classification of pancreatic fistula (Grades A – C). Patients who underwent other types of surgery than pancreato-duodenectomy with pancreato-jejunostomy (PDPJ) were not considered for the pancreatic fistula grading endpoint.

End point type	Secondary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	69		
Units: Subjects				
No fistula	26	31		
Grade A fistula	28	28		
Grade B fistula	13	7		
Grade C fistula	3	3		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - grading

Statistical analysis description:

For the pancreatic fistula formation grading (worst grading over all visits), absolute and relative numbers of patients per grade or class were summarized descriptively and compared between the two groups using Fisher tests.

Comparison groups	Tachosil v No Tachosil

Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5339
Method	Fisher exact

Secondary: Clavien-Dindo classification

End point title	Clavien-Dindo classification

End point description:

One secondary endpoint was surgery associated and any other perioperative complications according to the classification described by Clavien and Dindo. Clavien–Dindo grade missing for one patient.

End point type	Secondary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	70		
Units: Subjects				
no complications	17	20		
Grade I	13	12		
Grade II	21	19		
Grade III	18	14		
Grade IV	1	2		
Grade V	1	3		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - Clavien-Dindo

Statistical analysis description:

For the classification according to Clavien and Dindo (worst classification over all visits), absolute and relative numbers of patients per grade or class were summarized descriptively and compared between the two groups using Fisher tests.

Comparison groups	Tachosil v No Tachosil
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8394
Method	Fisher exact

Secondary: Drainage fluid

End point title	Drainage fluid

End point description:

The daily amount of fluid from the drainage at days 3, 5, 7, 9 and 11 (if applicable) was compared between groups. Daily amount of fluid from the drainage was calculated as the sum of the reported volume of both sides (left and right). These derived volumes per patient were aggregated for the predefined time points using the mean (or median, if applicable). Summary statistics were derived and descriptively compared between groups for the predefined time points.

End point type	Secondary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	67		
Units: ml				
median (full range (min-max))	318.5 (67.5 to 2090)	424 (86.7 to 4980)		

Attachments (see zip file)	170222_ABCSG P00_1_drainage volume plot.pdf

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - drainage fluid

Statistical analysis description:

The median per patient over all predefined time points for daily amount of fluid from the drainage, was also derived and compared between groups by Wilcoxon test.

Comparison groups	Tachosil v No Tachosil
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.156
Method	Wilcoxon (Mann-Whitney)

Secondary: Ex-drain site fluid

End point title	Ex-drain site fluid

End point description:

The daily amount of fluid from the ex drain site at days 3, 5, 7, 9 and 11 (if applicable) was compared between groups. The daily amount of fluid from the ex drain site was calculated as the sum of the reported volume of both sides (left and right). These derived volumes per patient were aggregated for the predefined time points using the mean (or median, if applicable). Summary statistics were derived and descriptively compared between groups for the predefined time points. Due to a huge amount of missing data (for some time points no data were available at all), only the time point with most available data (Day 9) is shown.

End point type	Secondary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: ml				
median (full range (min-max))	100 (0 to 660)	100 (1 to 1000)		

Attachments (see zip file)	170222_ABCSG P00_2_ex drainage volume plot.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Total drain amylase

End point title	Total drain amylase

End point description:

Daily content of drain amylase at days 3, 5, 7, 9 and 11 (if applicable) was compared between groups. For the content of amylase the maximum of both drainage sides was used at the patient level. Summary statistics were derived and descriptively compared between groups for the predefined time points.

End point type	Secondary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	48		
Units: U/L				
median (full range (min-max))	110.5 (5.3 to 24207)	90.5 (4 to 20537)		

Attachments (see zip file)	170222_ABCSG P00_3_total amylase plot.pdf

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - total drain amylase

Statistical analysis description:

The median per patient over all predefined time points for content of amylase was also derived and compared between groups with the Wilcoxon test.

Comparison groups	Tachosil v No Tachosil

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.494
Method	Wilcoxon (Mann-Whitney)

Secondary: Pancreatic specific drain amylase

End point title	Pancreatic specific drain amylase

End point description:

Daily content of drain amylase at days 3, 5, 7, 9 and 11 (if applicable) was compared between groups. For the content of amylase the maximum of both drainage sides was used at the patient level. Summary statistics were derived and descriptively compared between groups for the predefined time points.

End point type	Secondary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	37		
Units: U/L				
median (full range (min-max))	34 (1 to 5422.5)	38.5 (1 to 49919)		

Attachments (see zip file)	170222_ABCSG P00_4_pancreatic amylase plot.pdf

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - pancreatic amylase

Statistical analysis description:

The median per patient over all predefined time points for content of amylase was also derived and compared between groups with the Wilcoxon test.

Comparison groups	No Tachosil v Tachosil
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.632
Method	Wilcoxon (Mann-Whitney)

Secondary: Drain lipase

End point title	Drain lipase

End point description:

Daily content of drain lipase at days 3, 5, 7, 9 and 11 (if applicable) was compared between groups. For

the content of lipase the maximum of both drainage sides was used at the patient level. Summary statistics were derived and descriptively compared between groups for the predefined time points.

End point type	Secondary

End point timeframe:

During post surgery assessment starting from the third postoperative day.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	65		
Units: U/L				
median (full range (min-max))	267.3 (3 to 27390)	213.3 (3.6 to 145310)		

Attachments (see zip file)	170222_ABCSG P00_5_lipase plot.pdf

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - drain lipase

Statistical analysis description:

The median per patient over all predefined time points for content of lipase was also derived and compared between groups with the Wilcoxon test.

Comparison groups	Tachosil v No Tachosil
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.613
Method	Wilcoxon (Mann-Whitney)

Secondary: Time to drain removal

End point title	Time to drain removal

End point description:

The time (days) until drain removal was compared between groups.

End point type	Secondary

End point timeframe:

Time until drain removal.

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: days				
arithmetic mean (standard error)	11.56 (± 1.0)	13.28 (± 1.29)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - drainage removal
Statistical analysis description:	
The time (days) until drain removal was compared between groups by log-rank test.	
Comparison groups	Tachosil v No Tachosil
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6131
Method	Logrank

Secondary: Time to fistula closure

End point title	Time to fistula closure
End point description:	
The time (days) until fistula closure was compared between groups.	
End point type	Secondary
End point timeframe:	
Time until fistula closure.	

End point values	Tachosil	No Tachosil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	38		
Units: days				
arithmetic mean (standard error)	17.62 (± 2.23)	16.47 (± 2.14)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - fistula closure
Statistical analysis description:	
The time (days) until fistula closure was compared between groups by log-rank test.	
Comparison groups	Tachosil v No Tachosil

Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7397
Method	Logrank

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from ICF signature until 42 days after surgery	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	No Tachosil
Reporting group description: -	
Reporting group title	Tachosil
Reporting group description: -	

Serious adverse events	No Tachosil	Tachosil	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 71 (29.58%)	27 / 71 (38.03%)	
number of deaths (all causes)	4	1	
number of deaths resulting from adverse events	4	1	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence	Additional description: Abdominal wound dehiscence		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic fistula	Additional description: Anastomotic fistula		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic stenosis	Additional description: Anastomotic stenosis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to anastomose	Additional description: Failure to anastomose		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatic leak	Additional description: Pancreatic leak		
subjects affected / exposed	3 / 71 (4.23%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 12	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak	Additional description: Post procedural bile leak		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage	Additional description: Post procedural haemorrhage		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma	Additional description: Seroma		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma	Additional description: Haematoma		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic infarction	Additional description: Haemorrhagic infarction		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymphatic fistula	Additional description: Lymphatic fistula		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Nervous system disorders			
Parkinson's disease	Additional description: Parkinson's disease		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus	Additional description: Status epilepticus		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure	Additional description: Multi-organ failure		
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer	Additional description: Gastric ulcer		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coeliac artery compression syndrome	Additional description: Coeliac artery compression syndrome		

subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction	Additional description: Intestinal obstruction		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation	Additional description: Intestinal perforation		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage	Additional description: Intra-abdominal haemorrhage		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic fistula	Additional description: Pancreatic fistula		
subjects affected / exposed	2 / 71 (2.82%)	5 / 71 (7.04%)	
occurrences causally related to treatment / all	0 / 7	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage	Additional description: Upper gastrointestinal haemorrhage		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary fistula	Additional description: Biliary fistula		

subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis	Additional description: Cholangitis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic infarction	Additional description: Hepatic infarction		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome	Additional description: Acute respiratory distress syndrome		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	2 / 71 (2.82%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Abdominal abscess	Additional description: Abdominal abscess		
subjects affected / exposed	0 / 71 (0.00%)	4 / 71 (5.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess	Additional description: Abscess		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fungal sepsis	Additional description: Fungal sepsis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection	Additional description: Infection		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess	Additional description: Liver abscess		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration	Additional description: Dehydration		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid retention	Additional description: Fluid retention		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition	Additional description: Malnutrition		

subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	No Tachosil	Tachosil	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 71 (71.83%)	52 / 71 (73.24%)	
Vascular disorders			
Blood pressure fluctuation	Additional description: Blood pressure fluctuation		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Haematoma	Additional description: Haematoma		
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	
occurrences (all)	3	0	
Hot flush	Additional description: Hot flush		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Hypertension	Additional description: Hypertension		
subjects affected / exposed	4 / 71 (5.63%)	4 / 71 (5.63%)	
occurrences (all)	5	6	
Hypotension	Additional description: Hypotension		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	2	2	
Lymphatic fistula	Additional description: Lymphatic fistula		
subjects affected / exposed	2 / 71 (2.82%)	1 / 71 (1.41%)	
occurrences (all)	2	1	
Phlebitis	Additional description: Phlebitis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Shock haemorrhagic	Additional description: Shock haemorrhagic		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Pregnancy, puerperium and perinatal conditions			

Perineal haematoma	Additional description: Perineal haematoma		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Catheter site haematoma	Additional description: Catheter site haematoma		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Chills	Additional description: Chills		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	3	0	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	3	
Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Multi-organ failure	Additional description: Multi-organ failure		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	0 / 71 (0.00%)	3 / 71 (4.23%)	
occurrences (all)	0	4	
Oedema	Additional description: Oedema		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Pain	Additional description: Pain		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Pyrexia	Additional description: Pyrexia		

subjects affected / exposed	6 / 71 (8.45%)	4 / 71 (5.63%)	
occurrences (all)	8	10	
Systemic inflammatory response syndrome	Additional description: Systemic inflammatory response syndrome		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	2	4	
Cough	Additional description: Cough		
subjects affected / exposed	1 / 71 (1.41%)	3 / 71 (4.23%)	
occurrences (all)	2	4	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	4 / 71 (5.63%)	1 / 71 (1.41%)	
occurrences (all)	9	4	
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	6	
Psychiatric disorders			
Delirium	Additional description: Delirium		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Adjustment disorder with depressed mood	Additional description: Adjustment disorder with depressed mood		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Depressed mood	Additional description: Depressed mood		
subjects affected / exposed	0 / 71 (0.00%)	3 / 71 (4.23%)	
occurrences (all)	0	4	
Insomnia	Additional description: Insomnia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	

Depression	Additional description: Depression		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Korsakoff's syndrome	Additional description: Korsakoff's syndrome		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	2	2	
Panic attack	Additional description: Panic attack		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Restlessness	Additional description: Restlessness		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Sleep disorder	Additional description: Sleep disorder		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	2	1	
Tobacco withdrawal symptoms	Additional description: Tobacco withdrawal symptoms		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Investigations			
Enterococcus test positive	Additional description: Enterococcus test positive		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Bile output	Additional description: Bile output		
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Inflammatory marker increased	Additional description: Inflammatory marker increased		
subjects affected / exposed	5 / 71 (7.04%)	2 / 71 (2.82%)	
occurrences (all)	7	2	
Lipase increased	Additional description: Lipase increased		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Weight decreased	Additional description: Weight decreased		

subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence	Additional description: Abdominal wound dehiscence		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	4	2	
Anastomotic complication	Additional description: Anastomotic complication		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Anastomotic haemorrhage	Additional description: Anastomotic haemorrhage		
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	
occurrences (all)	5	0	
Excoriation	Additional description: Excoriation		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Hepatic haematoma	Additional description: Hepatic haematoma		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	1	1	
Incisional hernia	Additional description: Incisional hernia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Laceration	Additional description: Laceration		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Post procedural haematoma	Additional description: Post procedural haematoma		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Postoperative hernia	Additional description: Postoperative hernia		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	3	
Postoperative fever	Additional description: Postoperative fever		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	1	2	
Seroma	Additional description: Seroma		

subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	2	1	
Procedural pain	Additional description: Procedural pain		
subjects affected / exposed	1 / 71 (1.41%)	3 / 71 (4.23%)	
occurrences (all)	2	6	
Subcutaneous haematoma	Additional description: Subcutaneous haematoma		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Wound dehiscence	Additional description: Wound dehiscence		
subjects affected / exposed	0 / 71 (0.00%)	3 / 71 (4.23%)	
occurrences (all)	0	3	
Thermal burn	Additional description: Thermal burn		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Wound secretion	Additional description: Wound secretion		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	2	2	
Cardiac disorders			
Angina pectoris	Additional description: Angina pectoris		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	3	
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	2 / 71 (2.82%)	2 / 71 (2.82%)	
occurrences (all)	4	2	
Cyanosis	Additional description: Cyanosis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Long QT syndrome	Additional description: Long QT syndrome		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	3 / 71 (4.23%)	2 / 71 (2.82%)	
occurrences (all)	6	4	
Nervous system disorders			
Brain injury	Additional description: Brain injury		

subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Dizziness	Additional description: Dizziness		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Cerebral atrophy	Additional description: Cerebral atrophy		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Dysaesthesia	Additional description: Dysaesthesia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Headache	Additional description: Headache		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Intercostal neuralgia	Additional description: Intercostal neuralgia		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Leukoencephalopathy	Additional description: Leukoencephalopathy		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Paralysis	Additional description: Paralysis		
subjects affected / exposed	0 / 71 (0.00%)	3 / 71 (4.23%)	
occurrences (all)	0	4	
Parkinson's disease	Additional description: Parkinson's disease		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Presyncope	Additional description: Presyncope		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Syncope	Additional description: Syncope		

subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	7	0	
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	7 / 71 (9.86%)	6 / 71 (8.45%)	
occurrences (all)	8	13	
Anaemia folate deficiency	Additional description: Anaemia folate deficiency		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Coagulopathy	Additional description: Coagulopathy		
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	
occurrences (all)	3	0	
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Normochromic normocytic anaemia	Additional description: Normochromic normocytic anaemia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Splenic infarction	Additional description: Splenic infarction		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	3	
Ear and labyrinth disorders			
Vertigo	Additional description: Vertigo		
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	1	5	
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	0 / 71 (0.00%)	4 / 71 (5.63%)	
occurrences (all)	0	6	
Abnormal faeces	Additional description: Abnormal faeces		

subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	3	0	
Ascites	Additional description: Ascites		
subjects affected / exposed	0 / 71 (0.00%)	3 / 71 (4.23%)	
occurrences (all)	0	8	
Colitis	Additional description: Colitis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	10 / 71 (14.08%)	6 / 71 (8.45%)	
occurrences (all)	16	9	
Constipation	Additional description: Constipation		
subjects affected / exposed	2 / 71 (2.82%)	3 / 71 (4.23%)	
occurrences (all)	2	8	
Diverticulum oesophageal	Additional description: Diverticulum oesophageal		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	3	
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	2	2	
Faecal incontinence	Additional description: Faecal incontinence		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Flatulence	Additional description: Flatulence		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	1	2	
Faecaloma	Additional description: Faecaloma		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Gastric haemorrhage	Additional description: Gastric haemorrhage		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	3	0	
Gastric ulcer	Additional description: Gastric ulcer		

subjects affected / exposed	3 / 71 (4.23%)	1 / 71 (1.41%)	
occurrences (all)	5	1	
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	3	
Haemorrhoidal haemorrhage	Additional description: Haemorrhoidal haemorrhage		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Ileus	Additional description: Ileus		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Impaired gastric emptying	Additional description: Impaired gastric emptying		
subjects affected / exposed	1 / 71 (1.41%)	5 / 71 (7.04%)	
occurrences (all)	2	7	
Inguinal hernia	Additional description: Inguinal hernia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Nausea	Additional description: Nausea		
subjects affected / exposed	5 / 71 (7.04%)	3 / 71 (4.23%)	
occurrences (all)	8	4	
Melaena	Additional description: Melaena		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	4	0	
Oesophagitis	Additional description: Oesophagitis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	4	
Oral discomfort	Additional description: Oral discomfort		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Pancreatic necrosis	Additional description: Pancreatic necrosis		
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences (all)	0	5	
Pancreatitis	Additional description: Pancreatitis		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	1	1	
Subileus	Additional description: Subileus		

subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	3	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	4 / 71 (5.63%)	6 / 71 (8.45%)	
occurrences (all)	9	9	
Hepatobiliary disorders			
Cholestasis	Additional description: Cholestasis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Biliary fistula	Additional description: Biliary fistula		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Hepatic fibrosis	Additional description: Hepatic fibrosis		
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences (all)	0	2	
Hepatic necrosis	Additional description: Hepatic necrosis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Hepatic lesion	Additional description: Hepatic lesion		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	8	0	
Hepatic steatosis	Additional description: Hepatic steatosis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Hepatorenal syndrome	Additional description: Hepatorenal syndrome		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Alopecia areata	Additional description: Alopecia areata		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Blister	Additional description: Blister		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Decubitus ulcer	Additional description: Decubitus ulcer		

subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Dermatitis	Additional description: Dermatitis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact	Additional description: Dermatitis contact		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Drug eruption	Additional description: Drug eruption		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Eczema	Additional description: Eczema		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	1	3	
Erythema	Additional description: Erythema		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Rash	Additional description: Rash		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	1	2	
Intertrigo	Additional description: Intertrigo		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Skin erosion	Additional description: Skin erosion		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Urticaria	Additional description: Urticaria		
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences (all)	0	3	
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	
occurrences (all)	3	0	
Nephrolithiasis	Additional description: Nephrolithiasis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	

Leukocyturia	Additional description: Leukocyturia		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Endocrine disorders			
Goitre	Additional description: Goitre		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Hyperthyroidism	Additional description: Hyperthyroidism		
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Back pain	Additional description: Back pain		
subjects affected / exposed	1 / 71 (1.41%)	3 / 71 (4.23%)	
occurrences (all)	1	4	
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Infections and infestations			
Abdominal abscess	Additional description: Abdominal abscess		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	5	4	
Candidiasis	Additional description: Candidiasis		
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences (all)	0	3	
Clostridium difficile colitis	Additional description: Clostridium difficile colitis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	2	0	

Clostridium difficile infection	Additional description: Clostridium difficile infection		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Cystitis	Additional description: Cystitis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Device related infection	Additional description: Device related infection		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Douglas' abscess	Additional description: Douglas' abscess		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Enterococcal sepsis	Additional description: Enterococcal sepsis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Infection	Additional description: Infection		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Paronychia	Additional description: Paronychia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Perihepatic abscess	Additional description: Perihepatic abscess		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	4	0	
Peritonitis	Additional description: Peritonitis		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Pseudomonas infection	Additional description: Pseudomonas infection		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis	Additional description: Pyelonephritis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	

Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Sepsis	Additional description: Sepsis		
subjects affected / exposed	2 / 71 (2.82%)	1 / 71 (1.41%)	
occurrences (all)	3	1	
Septic shock	Additional description: Septic shock		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Staphylococcal infection	Additional description: Staphylococcal infection		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Staphylococcal sepsis	Additional description: Staphylococcal sepsis		
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences (all)	0	2	
Streptococcal bacteraemia	Additional description: Streptococcal bacteraemia		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	1	0	
Subcutaneous abscess	Additional description: Subcutaneous abscess		
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	
occurrences (all)	5	1	
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	6 / 71 (8.45%)	3 / 71 (4.23%)	
occurrences (all)	8	3	
Wound infection	Additional description: Wound infection		
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	
occurrences (all)	1	5	
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Fluid retention	Additional description: Fluid retention		

subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	
occurrences (all)	0	3	
Gout	Additional description: Gout		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	2 / 71 (2.82%)	1 / 71 (1.41%)	
occurrences (all)	4	3	
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	3 / 71 (4.23%)	0 / 71 (0.00%)	
occurrences (all)	6	0	
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	6 / 71 (8.45%)	6 / 71 (8.45%)	
occurrences (all)	8	7	
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	2	
Malnutrition	Additional description: Malnutrition		
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	
occurrences (all)	0	1	
Type 1 diabetes mellitus	Additional description: Type 1 diabetes mellitus		
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29664999