



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
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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@abcsbg.at
Scientific contact	Prof. Martin Schindl, ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsbg.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 pancreaticoduodenectomy 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
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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
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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/m ²			
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
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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
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Reporting group description:

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

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

Statistical analysis title	Secondary endpoint analysis - drain lipase
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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
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End point description:

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

End point type	Secondary
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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 (\pm 1.0)	13.28 (\pm 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 (\pm 2.23)	16.47 (\pm 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	No Tachosil
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Reporting group description: -

Reporting group title	Tachosil
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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			
	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
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
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
General disorders and administration site conditions			
	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
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
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
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
Gastrointestinal disorders			
	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
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
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
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 / 4

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 subjects affected / exposed occurrences (all)	Additional description: Perineal haematoma		
	1 / 71 (1.41%) 1	0 / 71 (0.00%) 0	
General disorders and administration site conditions			
	Additional description: Catheter site haematoma		
Catheter site haematoma subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1	0 / 71 (0.00%) 0	
Chills	Additional description: Chills		
	1 / 71 (1.41%) 3	0 / 71 (0.00%) 0	
Fatigue	Additional description: Fatigue		
	0 / 71 (0.00%) 0	1 / 71 (1.41%) 1	
General physical health deterioration	Additional description: General physical health deterioration		
	0 / 71 (0.00%) 0	1 / 71 (1.41%) 3	
Generalised oedema	Additional description: Generalised oedema		
	0 / 71 (0.00%) 0	1 / 71 (1.41%) 1	
Multi-organ failure	Additional description: Multi-organ failure		
	1 / 71 (1.41%) 1	0 / 71 (0.00%) 0	
Impaired healing	Additional description: Impaired healing		
	0 / 71 (0.00%) 0	1 / 71 (1.41%) 2	
Oedema peripheral	Additional description: Oedema peripheral		
	0 / 71 (0.00%) 0	3 / 71 (4.23%) 4	
Oedema	Additional description: Oedema		
	1 / 71 (1.41%) 2	0 / 71 (0.00%) 0	
Pain	Additional description: Pain		
	1 / 71 (1.41%) 1	0 / 71 (0.00%) 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	
Additional description: Gastrooesophageal reflux disease			
Gastrooesophageal reflux disease	0 / 71 (0.00%)	1 / 71 (1.41%)	
subjects affected / exposed			
occurrences (all)	0	3	
Additional description: Haemorrhoidal haemorrhage			
Haemorrhoidal haemorrhage	1 / 71 (1.41%)	0 / 71 (0.00%)	
subjects affected / exposed			
occurrences (all)	2	0	
Additional description: Ileus			
Ileus	1 / 71 (1.41%)	0 / 71 (0.00%)	
subjects affected / exposed			
occurrences (all)	1	0	
Additional description: Impaired gastric emptying			
Impaired gastric emptying	1 / 71 (1.41%)	5 / 71 (7.04%)	
subjects affected / exposed			
occurrences (all)	2	7	
Additional description: Inguinal hernia			
Inguinal hernia	1 / 71 (1.41%)	0 / 71 (0.00%)	
subjects affected / exposed			
occurrences (all)	1	0	
Additional description: Nausea			
Nausea	5 / 71 (7.04%)	3 / 71 (4.23%)	
subjects affected / exposed			
occurrences (all)	8	4	
Additional description: Melaena			
Melaena	1 / 71 (1.41%)	0 / 71 (0.00%)	
subjects affected / exposed			
occurrences (all)	4	0	
Additional description: Oesophagitis			
Oesophagitis	0 / 71 (0.00%)	1 / 71 (1.41%)	
subjects affected / exposed			
occurrences (all)	0	4	
Additional description: Oral discomfort			
Oral discomfort	0 / 71 (0.00%)	1 / 71 (1.41%)	
subjects affected / exposed			
occurrences (all)	0	1	
Additional description: Pancreatic necrosis			
Pancreatic necrosis	0 / 71 (0.00%)	2 / 71 (2.82%)	
subjects affected / exposed			
occurrences (all)	0	5	
Additional description: Pancreatitis			
Pancreatitis	1 / 71 (1.41%)	1 / 71 (1.41%)	
subjects affected / exposed			
occurrences (all)	1	1	
Additional description: Subileus			
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 subjects affected / exposed occurrences (all)	Additional description: Leukocyturia		
	0 / 71 (0.00%) 0	1 / 71 (1.41%) 1	
Pollakiuria subjects affected / exposed occurrences (all)	Additional description: Pollakiuria		
	1 / 71 (1.41%) 2	0 / 71 (0.00%) 0	
Endocrine disorders Goitre subjects affected / exposed occurrences (all) Hyperthyroidism subjects affected / exposed occurrences (all)	Additional description: Goitre		
	1 / 71 (1.41%) 1	0 / 71 (0.00%) 0	
	Additional description: Hyperthyroidism		
	0 / 71 (0.00%) 0	2 / 71 (2.82%) 2	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Musculoskeletal pain subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	Additional description: Arthralgia		
	1 / 71 (1.41%) 2	0 / 71 (0.00%) 0	
	Additional description: Musculoskeletal pain		
	1 / 71 (1.41%) 1	0 / 71 (0.00%) 0	
	Additional description: Back pain		
	1 / 71 (1.41%) 1	3 / 71 (4.23%) 4	
	Additional description: Pain in extremity		
	0 / 71 (0.00%) 0	1 / 71 (1.41%) 1	
Infections and infestations Abdominal abscess subjects affected / exposed occurrences (all) Candidiasis subjects affected / exposed occurrences (all) Clostridium difficile colitis subjects affected / exposed occurrences (all)	Additional description: Abdominal abscess		
	1 / 71 (1.41%) 5	2 / 71 (2.82%) 4	
	Additional description: Candidiasis		
	0 / 71 (0.00%) 0	2 / 71 (2.82%) 3	
	Additional description: Clostridium difficile colitis		
	1 / 71 (1.41%) 2	0 / 71 (0.00%) 0	

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

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