Clinical trial results:
PeriOperative ISchemic Evaluation-3 (POISE-3) Trial

Summary

EudraCT number	2018-000539-29
Trial protocol	BE DK AT NL IT
Global end of trial date	03 February 2023

Results information

Result version number	v1 (current)
This version publication date	15 February 2025
First version publication date	15 February 2025

Trial information

Trial identification

Sponsor protocol code	2018.02.08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03505723
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Population Health Research Institute
Sponsor organisation address	20 Copeland Avenue, Hamilton, Canada,
Public contact	POISE-3 Project Office, Population Health Research Institute, 001 905-521-2100x4063, poise3@phri.ca
Scientific contact	POISE-3 Project Office, Population Health Research Institute, 001 905-521-2100x4063, poise3@phri.ca

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	28 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 November 2021
Global end of trial reached?	Yes
Global end of trial date	03 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if TXA is superior to placebo for the occurrence of life-threatening, major, and critical organ bleeding, and non-inferior to placebo for the occurrence of major arterial and venous thrombotic events; and to determine the impact of a hypotension-avoidance strategy versus a hypertension-avoidance strategy on the risk of major vascular events in patients who are followed for 30 days after noncardiac surgery.

Protection of trial subjects:

An independent data and safety monitoring committee reviewed interim analyses when 25%, 50%, and 75% of the 30-day data were available.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2018
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	Netherlands: 172
Country: Number of subjects enrolled	Poland: 143
Country: Number of subjects enrolled	Spain: 753
Country: Number of subjects enrolled	United Kingdom: 76
Country: Number of subjects enrolled	Austria: 84
Country: Number of subjects enrolled	Belgium: 152
Country: Number of subjects enrolled	Denmark: 130
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 133
Country: Number of subjects enrolled	Italy: 284
Country: Number of subjects enrolled	Australia: 573
Country: Number of subjects enrolled	Brazil: 71
Country: Number of subjects enrolled	Canada: 1916
Country: Number of subjects enrolled	Chile: 107
Country: Number of subjects enrolled	China: 425
Country: Number of subjects enrolled	India: 631
Country: Number of subjects enrolled	Malaysia: 654
Country: Number of subjects enrolled	New Zealand: 167
Country: Number of subjects enrolled	Pakistan: 128

Country: Number of subjects enrolled	Russian Federation: 1859
Country: Number of subjects enrolled	South Africa: 25
Country: Number of subjects enrolled	United States: 1045
Worldwide total number of subjects	9535
EEA total number of subjects	1858

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)	2790
From 65 to 84 years	6314
85 years and over	431

Subject disposition

Recruitment

Recruitment details:

We recruited patients from June 2018 through July 2021 at 114 hospitals in 22 countries. We randomly assigned 9535 patients to receive tranexamic acid (4757 patients) or placebo (4778 patients) The 30-day follow-up visit was completed for 99.9% of the patients.

Pre-assignment

Screening details:

26,581 were screened and eligible patients. Out of this number 17,046 eligible patients were not randomized. 5970 Patients did not consent; 3544 Physician declined to have patient participate; 4453 Research or staff unavailable; 925 not eligible for BP management arm; 520 Language barrier and 1634 were classified as other.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Randomization was performed by a central computerized system with the use of block randomization, with stratification according to center. Patients were assigned in a 1:1 ratio to receive tranexamic acid or placebo at the start and end of surgery and, in a 1:1 ratio with the use of a partial factorial design, to a hypotension-avoidance strategy or a hypertension-avoidance strategy. Patients, providers, data collectors, and outcome adjudicators were unaware of the trial-group assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tranexamic acid (active)

Arm description:

1g bolus/infusion within 20 minutes preceding anticipated skin incision, 1g bolus/infusion at surgery end when closing the wound

Arm type	Active comparator
Investigational medicinal product name	Tranexamic acid (active)
Investigational medicinal product code	
Other name	TXA
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

1g bolus/infusion within 20 minutes preceding anticipated skin incision, 1g bolus/infusion at surgery end when closing the wound

Arm title	Tranexamic acid (placebo)

Arm description:

0.9% normal saline bolus/infusion within 20 minutes preceding anticipated skin incision, at surgery end when closing the wound

Arm type	Placebo
Investigational medicinal product name	Tranexamic acid (placebo)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

0.9% normal saline bolus/infusion within 20 minutes preceding anticipated skin incision, at surgery end

when closing the wound

Number of subjects in period 1	Tranexamic acid (active)	Tranexamic acid (placebo)
Started	4757	4778
Completed	4757	4778

Baseline characteristics

Reporting groups	
Reporting group title	Tranexamic acid (active)
Reporting group description:	
1g bolus/infusion within 20 minutes preceding anticipated skin incision, 1g bolus/infusion at surgery end when closing the wound	
Reporting group title	Tranexamic acid (placebo)
Reporting group description:	
0.9% normal saline bolus/infusion within 20 minutes preceding anticipated skin incision, at surgery end when closing the wound	

Reporting group values	Tranexamic acid (active)	Tranexamic acid (placebo)	Total
Number of subjects	4757	4778	9535
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)	1387	1403	2790
From 65-84 years	3140	3174	6314
85 years and over	230	201	431
Age continuous Units: years			
arithmetic mean	69.49	69.29	
standard deviation	± 9.45	± 9.36	-
Gender categorical Units: Subjects			
Female	2088	2097	4185
Male	2669	2681	5350
Eligibility criteria met: History of coronary artery disease Units: Subjects			
Yes	1410	1466	2876
No	3347	3312	6659
Eligibility criteria met: History of peripheral artery disease Units: Subjects			
Yes	714	722	1436
No	4043	4056	8099
Eligibility criteria met: History of stroke Units: Subjects			
Yes	400	388	788
No	4357	4390	8747
Eligibility criteria met: Undergoing major vascular surgery			

Units: Subjects			
Yes	541	544	1085
No	4216	4234	8450
Risk criteria: Met ≥3 of 9 criteria Units: Subjects			
Yes	3988	4003	7991
No	769	775	1544
Risk criteria: Undergoing major surgery Units: Subjects			
Yes	3741	3798	7539
No	1016	980	1996
Risk criteria: Undergoing urgent or emergency surgery Units: Subjects			
Yes	555	540	1095
No	4202	4238	8440
Risk criteria: Age ≥70 yr Units: Subjects			
Yes	2611	2588	5199
No	2146	2190	4336
Risk criteria: Current diabetes for which medication is taken Units: Subjects			
Yes	1749	1812	3561
No	3008	2966	5974
Risk criteria: Preoperative serum creatinine level >175 µmol/liter Units: Subjects			
Yes	57	73	130
No	4700	4705	9405
Risk criteria: History of congestive heart failure Units: Subjects			
Yes	674	671	1345
No	4083	4107	8190
Risk criteria: History of transient ischemic attack Units: Subjects			
Yes	282	247	529
No	4475	4531	9006
Risk criteria: History of hypertension Units: Subjects			
Yes	4293	4321	8614
No	464	457	921
Risk criteria: History of smoking within 2 yr before surgery Units: Subjects			
Yes	1131	1128	2259
No	3626	3650	7276
Other medical history: Atrial fibrillation Units: Subjects			
Yes	478	445	923
No	4279	4333	8612

Other medical history: Active cancer Units: Subjects			
Yes	1311	1360	2671
No	3446	3418	6864

End points

End points reporting groups

Reporting group title	Tranexamic acid (active)
Reporting group description:	
1g bolus/infusion within 20 minutes preceding anticipated skin incision, 1g bolus/infusion at surgery end when closing the wound	
Reporting group title	Tranexamic acid (placebo)
Reporting group description:	
0.9% normal saline bolus/infusion within 20 minutes preceding anticipated skin incision, at surgery end when closing the wound	

Primary: Primary End Point

End point title	Primary End Point
End point description:	
End point type	Primary
End point timeframe:	
>	

End point values	Tranexamic acid (active)	Tranexamic acid (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4757	4778		
Units: Subjects				
Primary efficacy outcome: composite bleeding	433	561		
Primary safety outcome: composite cardiovascular	649	639		
MINS	608	602		
Nonhemorrhagic stroke	24	16		
Peripheral arterial thrombosis	22	23		
Symptomatic proximal venous thromboembolism	32	28		

Statistical analyses

Statistical analysis title	Primary efficacy outcome
Statistical analysis description:	
Composite bleeding outcome	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)

Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.87

Statistical analysis title	Primary safety outcome
Statistical analysis description: Composite cardiovascular outcome	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.04
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.14

Statistical analysis title	Components of composite cardiovascular outcome 1
Statistical analysis description: Individual components of composite cardiovascular outcome: MINS	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.14

Statistical analysis title	Components of composite cardiovascular outcome 2
Statistical analysis description: Individual components of composite cardiovascular outcome: Nonhemorrhagic stroke	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	2.84

Statistical analysis title	Components of composite cardiovascular outcome 3
Statistical analysis description: Individual components of composite cardiovascular outcome: Peripheral arterial thrombosis	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.72

Statistical analysis title	Components of composite cardiovascular outcome 4
Statistical analysis description: Individual components of composite cardiovascular outcome: Symptomatic proximal venous thromboembolism	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.91

Secondary: Secondary End Point

End point title	Secondary End Point
End point description:	
End point type	Secondary
End point timeframe:	
>	

End point values	Tranexamic acid (active)	Tranexamic acid (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4757	4778		
Units: Subjects				
Bleeding independently assoc w death after NC Surg	416	541		
MINS not fulfilling the universal def of MI	549	549		
Myocardial infarction	67	53		
Net risk–benefit outcome	983	1046		
Life-threatening bleeding	78	79		
Major bleeding	363	496		
Bleeding into a critical organ	12	21		

Statistical analyses

Statistical analysis title	Other secondary outcomes 1
Statistical analysis description:	
Bleeding independently associated with death after noncardiac surgery	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.87

Statistical analysis title	Other secondary outcomes 2
Statistical analysis description: MINS not fulfilling the universal definition of myocardial infarction	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.13

Statistical analysis title	Other secondary outcomes 3
Statistical analysis description: Myocardial infarction	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.82

Statistical analysis title	Other secondary outcomes 4
Statistical analysis description: Net risk–benefit outcome	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.02

Statistical analysis title	Indiv. components of composite bleeding outcome 1
Statistical analysis description: Life-threatening bleeding	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.36

Statistical analysis title	Indiv. components of composite bleeding outcome 1
Statistical analysis description: Major bleeding	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.83

Statistical analysis title	Indiv. components of composite bleeding outcome 3
Statistical analysis description: Bleeding into a critical organ	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)

Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	1.16

Other pre-specified: Tertiary Outcomes

End point title	Tertiary Outcomes

End point description:

End point type	Other pre-specified

End point timeframe:

>

End point values	Tranexamic acid (active)	Tranexamic acid (placebo)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4757	4778		
Units: Subjects				
Major bleeding according to ISTH criteria	315	415		
Transfusion of ≥1 unit of packed red cells	449	574		
Death from any cause	52	57		
Death from cardiovascular cause	25	30		
Hemorrhagic stroke	2	0		
Amputation	14	21		
Symptomatic pulmonary embolism	24	17		
Symptomatic proximal deep venous thrombosis	11	13		
(a)symptomatic proximal venous thromboembolism	32	28		
Cardiac revascularization	12	13		
Acute kidney injury	672	655		
New renal-replacement therapy	19	16		
Rehospitalization for cardiovascular reasons	84	75		
Seizure	10	3		
Infection	499	487		
Sepsis	68	63		
Disability	1408	1407		

Statistical analyses

Statistical analysis title	Tertiary outcome 1
Statistical analysis description: Major bleeding according to ISTH criteria	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.87

Statistical analysis title	Tertiary outcome 2
Statistical analysis description: Transfusion of ≥1 unit of packed red cells	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.88

Statistical analysis title	Tertiary outcome 3
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)

Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.33

Statistical analysis title	Tertiary outcome 4
Statistical analysis description: Death from cardiovascular cause	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.42

Statistical analysis title	Tertiary outcome 6
Statistical analysis description: Amputation	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.31

Statistical analysis title	Tertiary outcome 7
Statistical analysis description: Symptomatic pulmonary embolism	

Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.64

Statistical analysis title	Tertiary outcome 8
Statistical analysis description:	
Symptomatic proximal deep venous thrombosis	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.9

Statistical analysis title	Tertiary outcome 9
Statistical analysis description:	
Any symptomatic or asymptomatic proximal venous thromboembolism	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.91

Statistical analysis title	Tertiary outcome 10

Statistical analysis description: Cardiac revascularization	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	2.03

Statistical analysis title	Tertiary outcome 11
Statistical analysis description: Acute kidney injury	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.15

Statistical analysis title	Tertiary outcome 13
Statistical analysis description: Rehospitalization for cardiovascular reasons	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.54

Statistical analysis title	Tertiary outcome 14
Statistical analysis description: Seizure	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	3.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	12.2

Statistical analysis title	Tertiary outcome 15
Statistical analysis description: Infection	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.17

Statistical analysis title	Tertiary outcome 16
Statistical analysis description: Sepsis	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.53

Statistical analysis title	Tertiary outcome 19
Statistical analysis description: Disability	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.13

Statistical analysis title	Tertiary outcome 12
Statistical analysis description: New renal-replacement therapy	
Comparison groups	Tranexamic acid (active) v Tranexamic acid (placebo)
Number of subjects included in analysis	9535
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	2.32

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

There are no non-serious adverse events recorded for these results.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Tranexamic acid (active)

Reporting group description:

1g bolus/infusion within 20 minutes preceding anticipated skin incision, 1g bolus/infusion at surgery end when closing the wound

Reporting group title	Placebo (active)

Reporting group description:

0.9% normal saline bolus/infusion within 20 minutes preceding anticipated skin incision, at surgery end when closing the wound

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Given the well-established safety profile of the study drug and the primary focus on evaluating serious adverse events, this clinical trial did not systematically collect data on non-serious adverse events, as they are unlikely to provide significant information regarding the drug's safety concerns in this study population.

Serious adverse events	Tranexamic acid (active)	Placebo (active)	
Total subjects affected by serious adverse events			
subjects affected / exposed	263 / 4757 (5.53%)	242 / 4778 (5.06%)	
number of deaths (all causes)	52	57	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	3 / 4757 (0.06%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myelomonocytic leukemia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	1 / 4757 (0.02%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the hypopharynx			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal gland cancer metastatic			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastasis			
subjects affected / exposed	1 / 4757 (0.02%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer stage I			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary renal cell carcinoma			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma metastatic			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hematoma			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	5 / 4757 (0.11%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 4757 (0.02%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	4 / 4757 (0.08%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	2 / 4757 (0.04%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischemia			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry gangrene			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemodynamic instability			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic occlusion			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brachiocephalic vein thrombosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphatic fistula			
subjects affected / exposed	2 / 4757 (0.04%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granulomatosis with polyangiitis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein stenosis			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atheroembolism			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Pituitary tumor removal			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoma excision			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal anastomosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal resection			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral prostatectomy			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrostomy			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteral stent removal			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter placement			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter removal			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileocolostomy			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal anastomosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia repair			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve repair			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central venous catheter removal			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drain removal			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eventration repair			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalized edema			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Edema			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Edema peripheral			
subjects affected / exposed	2 / 4757 (0.04%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			

subjects affected / exposed	4 / 4757 (0.08%)	5 / 4778 (0.10%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyp			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site discharge			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehiscence			
subjects affected / exposed	2 / 4757 (0.04%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Female genital tract fistula			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 4757 (0.06%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnea			

subjects affected / exposed	3 / 4757 (0.06%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemoptysis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 4757 (0.04%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal edema			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	5 / 4757 (0.11%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	4 / 4757 (0.08%)	4 / 4778 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory depression			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 4757 (0.04%)	5 / 4778 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Negative pressure pulmonary edema			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	4 / 4757 (0.08%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device leakage			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device loosening			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Autoimmune hepatitis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	4 / 4757 (0.08%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis alcoholic			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver injury			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood glucose increased			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure abnormal			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose fluctuation			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulation test abnormal			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nutritional condition abnormal			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SARS-CoV-2 test positive			

subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns third degree			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	5 / 4757 (0.11%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 4757 (0.04%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve injury			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 4757 (0.02%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric injury			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	6 / 4757 (0.13%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suture rupture			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic leak			
subjects affected / exposed	3 / 4757 (0.06%)	4 / 4778 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prescribed overdose			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	37 / 4757 (0.78%)	30 / 4778 (0.63%)	
occurrences causally related to treatment / all	0 / 37	0 / 30	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural diarrhea			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			

subjects affected / exposed	1 / 4757 (0.02%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural hypotension			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic leak			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dural tear			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site inflammation			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation sickness syndrome			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprosthetic fracture			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic lung injury			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fascial rupture			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal injury			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated parastomal hernia			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diversion colitis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
11-beta-hydroxylase deficiency			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheo-esophageal fistula			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycinemia			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 4757 (0.04%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodal arrhythmia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery thrombosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 4757 (0.02%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycemic encephalopathy			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve palsy			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	7 / 4757 (0.15%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischemic attack			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual field defect			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anemia			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness transient			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 4757 (0.13%)	5 / 4778 (0.10%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal stenosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ascites			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	4 / 4757 (0.08%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal obstruction			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocele			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal fistula			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal hemorrhage			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematemesis			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal stenosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 4757 (0.02%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischemia			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	10 / 4757 (0.21%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 10	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal pseudo-obstruction			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal stenosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malabsorption			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Esophageal stenosis			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Esophagitis			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	2 / 4757 (0.04%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal prolapse			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	13 / 4757 (0.27%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 13	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal hemorrhage			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal edema			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngo-esophageal diverticulum			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal fluid collection			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal hemorrhage			
subjects affected / exposed	1 / 4757 (0.02%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous emphysema			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient acantholytic dermatosis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hematuria			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 4757 (0.02%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric stenosis			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder hemorrhage			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	7 / 4757 (0.15%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinoma			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal mass			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	16 / 4757 (0.34%)	9 / 4778 (0.19%)	
occurrences causally related to treatment / all	0 / 16	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 4757 (0.06%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 4757 (0.06%)	5 / 4778 (0.10%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Compartment syndrome			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemarthrosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle atrophy			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 4757 (0.04%)	3 / 4778 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudarthrosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 4757 (0.06%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex encephalitis			

subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 4757 (0.04%)	6 / 4778 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	2 / 4757 (0.04%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			

subjects affected / exposed	0 / 4757 (0.00%)	2 / 4778 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycemia			
subjects affected / exposed	3 / 4757 (0.06%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalemia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycemia			
subjects affected / exposed	1 / 4757 (0.02%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalemia			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatremia			
subjects affected / exposed	3 / 4757 (0.06%)	7 / 4778 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding intolerance			

subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adult failure to thrive			
subjects affected / exposed	1 / 4757 (0.02%)	0 / 4778 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Starvation ketoacidosis			
subjects affected / exposed	0 / 4757 (0.00%)	1 / 4778 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tranexamic acid (active)	Placebo (active)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4757 (0.00%)	0 / 4778 (0.00%)	

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