Clinical trial results:
STOPAH: STeroids Or Pentoxifylline for Alcoholic Hepatitis

Summary

EudraCT number	2009-013897-42
Trial protocol	GB
Global end of trial date	25 April 2014

Results information

Result version number	v1 (current)
This version publication date	07 February 2022
First version publication date	07 February 2022

Trial information

Trial identification

Sponsor protocol code	RHMMED0883

Additional study identifiers

ISRCTN number	ISRCTN88782125
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	MHRA CTA reference number: 11709/0227/001-0001

Notes:

Sponsors

Sponsor organisation name	University Hospital Southampton NHS Foundation Trust
Sponsor organisation address	Southampton General Hospital, Level E, Laboratory & Pathology Block, SCBR, MP 138, Southampton, United Kingdom, SO16 6YD
Public contact	University of Southampton Clinical Trials Unit, University of Southampton Clinical Trials Unit, 0044 2381205154, ctu@soton.ac.uk
Scientific contact	University of Southampton Clinical Trials Unit, University of Southampton Clinical Trials Unit, 0044 2381205154, ctu@soton.ac.uk

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	12 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 April 2014
Global end of trial reached?	Yes
Global end of trial date	25 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether prednisolone or pentoxifylline improve the 28 day mortality (death rate) from severe alcoholic hepatitis.
Link to the protocol:
https://www.nejm.org/doi/suppl/10.1056/NEJMoa1412278/suppl_file/nejmoa1412278_protocol.pdf

Protection of trial subjects:

See protocol - Link to the protocol:
https://www.nejm.org/doi/suppl/10.1056/NEJMoa1412278/suppl_file/nejmoa1412278_protocol.pdf

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 January 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 1092
Worldwide total number of subjects	1092
EEA total number of subjects	1092

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)	1019
From 65 to 84 years	73

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from January 2011 through February 2014 at 66 hospitals across the United Kingdom. In total, 66 trial sites were opened but subsequently, one site was closed after failing to recruit any patients.

Pre-assignment

Screening details:

A total of 5234 patients were screened for the trial, and after applying inclusion and exclusion criteria, 1103 were randomised and evenly allocated to the four treatment arms. 1092 patients started the trial.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Placebo

Arm description:

All patients were given one capsule containing placebo four times per day. The medication were administered for 28 days

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All patients were given one capsule placebo four times per day. The medication were administered for 28 days

Arm title	Placebo/Pred

Arm description:

All patients were given one capsule placebo three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo one capsule three times daily for 28 days

Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Prednisolone was given 40 mg daily for 28 days

Arm title	PTX/Placebo

Arm description:

All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule placebo once daily. Both medications were administered for 28 days

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All patients were given one capsule placebo once per day. The medication was administered for 28 days

Investigational medicinal product name	Pentoxifylline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

All patients were given one capsule containing 400 mg of PTX three times per day, administered for 28 days

Arm title	PTX/Pred

Arm description:

All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days.

Arm type	Experimental
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Prednisolone was given 40 mg daily for 28 days

Investigational medicinal product name	Pentoxifylline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pentoxifylline one capsule (400mg) tds for 28 days

Number of subjects in period 1	Placebo/Placebo	Placebo/Pred	PTX/Placebo
Started	272	274	273
Completed	192	190	184
Not completed	80	84	89
Consent withdrawn by subject	8	8	12
Early cessation of follow-up	48	-	-
Early cessation of follow-up	-	44	56
Lost to follow-up	24	32	21
Died before randomisation	-	-	-

Number of subjects in period 1	PTX/Pred
Started	273
Completed	181
Not completed	92
Consent withdrawn by subject	12
Early cessation of follow-up	-
Early cessation of follow-up	44
Lost to follow-up	35
Died before randomisation	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo/Placebo
Reporting group description:	
All patients were given one capsule containing placebo four times per day. The medication were administered for 28 days	
Reporting group title	Placebo/Pred
Reporting group description:	
All patients were given one capsule placebo three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days	
Reporting group title	PTX/Placebo
Reporting group description:	
All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule placebo once daily. Both medications were administered for 28 days	
Reporting group title	PTX/Pred
Reporting group description:	
All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days.	

Reporting group values	Placebo/Placebo	Placebo/Pred	PTX/Placebo
Number of subjects	272	274	273
Age categorical Units: Subjects			
Adults (18-64 years)	253	254	259
Adults 65-84 years	19	20	14
Age continuous Units: years			
arithmetic mean	48.8	49.3	47.9
standard deviation	± 10.3	± 10.6	± 10.2
Gender categorical Units: Subjects			
Female	110	97	109
Male	162	177	164

Reporting group values	PTX/Pred	Total	
Number of subjects	273	1092	
Age categorical Units: Subjects			
Adults (18-64 years)	253	1019	
Adults 65-84 years	20	73	
Age continuous Units: years			
arithmetic mean	48.6		
standard deviation	± 9.8	-	
Gender categorical Units: Subjects			
Female	91	407	
Male	182	685	

End points

End points reporting groups

Reporting group title	Placebo/Placebo
Reporting group description:	
All patients were given one capsule containing placebo four times per day. The medication were administered for 28 days	
Reporting group title	Placebo/Pred
Reporting group description:	
All patients were given one capsule placebo three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days	
Reporting group title	PTX/Placebo
Reporting group description:	
All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule placebo once daily. Both medications were administered for 28 days	
Reporting group title	PTX/Pred
Reporting group description:	
All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days.	
Subject analysis set title	Prednisolone at day 28
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
mortality among patients who received prednisolone those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at day 28	
Subject analysis set title	No Prednisolone at day 28
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
mortality among patients who didn`t receive prednisolone at 28 days	
Subject analysis set title	No Prednisolone at day 90
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
mortality among patients who didn`t receive prednisolone at 90 days	
Subject analysis set title	No Prednisolone at year 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
mortality among patients who didn`t receive prednisolone at 1 year	
Subject analysis set title	Prednisolone at day 90
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
mortality among patients who received prednisolone those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at day 90	
Subject analysis set title	Prednisolone at year 1
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
mortality among patients who received prednisolone those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at year 1	
Subject analysis set title	Pentoxifylline at day 28
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
mortality among patients who received pentoxifylline those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at day 28	
Subject analysis set title	Pentoxifylline at day 90
Subject analysis set type	Intention-to-treat

Subject analysis set description:

mortality among patients who received pentoxifylline those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at day 90

Subject analysis set title	Pentoxifylline at year 1
Subject analysis set type	Intention-to-treat

Subject analysis set description:

mortality among patients who received pentoxifylline those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at year 1

Subject analysis set title	No Pentoxifylline at day 28
Subject analysis set type	Intention-to-treat

Subject analysis set description:

mortality among patients who didn`t received pentoxifylline at day 28

Subject analysis set title	No Pentoxifylline at day 90
Subject analysis set type	Intention-to-treat

Subject analysis set description:

mortality among patients who didn`t receive pentoxifylline at day 90

Subject analysis set title	No Pentoxifylline at year 1
Subject analysis set type	Intention-to-treat

Subject analysis set description:

mortality among patients who didn`t receive pentoxifylline at year 1

Primary: Mortality at day 28

End point title	Mortality at day 28

End point description:

End point type	Primary

End point timeframe:

28 days

End point values	Placebo/Placebo	Placebo/Pred	PTX/Placebo	PTX/Pred
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	269	266	258	260
Units: participants who died	45	38	50	35

Statistical analyses

Statistical analysis title	Treatment interaction between predinosolone-pent

Statistical analysis description:

Treatment interaction between predinosolone-pentoxifylline group

Comparison groups	PTX/Placebo v Placebo/Pred v PTX/Pred

Number of subjects included in analysis	784
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.41
Method	Regression, Logistic

Primary: Mortality Prednisolone at day 28

End point title	Mortality Prednisolone at day 28

End point description:

End point type	Primary

End point timeframe:

28 days

End point values	Prednisolone at day 28	No Prednisolone at day 28		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	526	527		
Units: number of participants dies or liver tra	73	95		

Statistical analyses

Statistical analysis title	Prednisolone at days 28
Comparison groups	Prednisolone at day 28 v No Prednisolone at day 28
Number of subjects included in analysis	1053
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.06
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.01

Primary: Mortality Pentoxifylline at day 28

End point title	Mortality Pentoxifylline at day 28

End point description:

End point type	Primary

End point timeframe:

28 days

End point values	Pentoxifylline at day 28	No Pentoxifylline at day 28		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	518	535		
Units: number of participants dies or liver tra	85	83		

Statistical analyses

Statistical analysis title	Pentoxifylline at days 28
Comparison groups	Pentoxifylline at day 28 v No Pentoxifylline at day 28
Number of subjects included in analysis	1053
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.69
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.49

Secondary: Mortality or liver transplant at day 90 Prednisolone

End point title	Mortality or liver transplant at day 90 Prednisolone

End point description:

End point type	Secondary

End point timeframe:

90 days

End point values	No Prednisolone at day 90	Prednisolone at day 90		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	484	484		
Units: number of participants dies or liver tra	141	144		

Statistical analyses

Statistical analysis title	Prednisolone at days 90
Comparison groups	No Prednisolone at day 90 v Prednisolone at day 90
Number of subjects included in analysis	968
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.87
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.35

Secondary: Mortality or liver transplant at year 1 Prednisolone

End point title	Mortality or liver transplant at year 1 Prednisolone
End point description:	
End point type	Secondary
End point timeframe:	
1 year	

End point values	No Prednisolone at year 1	Prednisolone at year 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	376	371		
Units: number of participants dies or liver tra	211	210		

Statistical analyses

Statistical analysis title	Prednisolone at year 1
Comparison groups	No Prednisolone at year 1 v Prednisolone at year 1
Number of subjects included in analysis	747
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.94
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.35

Secondary: Mortality or liver transplant at day 90 Pentoxifylline	
End point title	Mortality or liver transplant at day 90 Pentoxifylline
End point description:	
End point type	Secondary
End point timeframe:	
90 days	

End point values	Pentoxifylline at day 90	No Pentoxifylline at day 90		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	478	490		
Units: number of participants dies or liver tra	139	146		

Statistical analyses

Statistical analysis title	Pentoxifylline at days 90
Comparison groups	Pentoxifylline at day 90 v No Pentoxifylline at day 90
Number of subjects included in analysis	968
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.81
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.97

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.28

Secondary: Mortality or liver transplant at year 1 Pentoxifylline

End point title	Mortality or liver transplant at year 1 Pentoxifylline
End point description:	

End point type	Secondary
End point timeframe:	
1 year	

End point values	Pentoxifylline at year 1	No Pentoxifylline at year 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	365	382		
Units: number of participants dies or liver tra	205	216		

Statistical analyses

Statistical analysis title	Pentoxifylline at year 1
Comparison groups	Pentoxifylline at year 1 v No Pentoxifylline at year 1
Number of subjects included in analysis	747
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.97
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.33

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
1 year	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Placebo/Placebo
Reporting group description: -	
Reporting group title	Placebo/Pred.
Reporting group description: -	
Reporting group title	PTX/Placebo
Reporting group description: -	
Reporting group title	PTX/Pred.
Reporting group description: -	

Serious adverse events	Placebo/Placebo	Placebo/Pred.	PTX/Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	106 / 273 (38.83%)	128 / 273 (46.89%)	111 / 272 (40.81%)
number of deaths (all causes)	44	53	43
number of deaths resulting from adverse events	44	53	43
Vascular disorders			
Thromboembolic event	Additional description: Thromboembolic event		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hematoma	Additional description: Hematoma		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Edema limbs	Additional description: Edema limbs		

subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure	Additional description: Multi-organ failure		
subjects affected / exposed	6 / 273 (2.20%)	3 / 273 (1.10%)	6 / 272 (2.21%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 4	0 / 3	0 / 3
General disorders and administration site conditions: Other, specify	Additional description: General disorders and administration site conditions: Other, specify		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise	Additional description: Malaise		
subjects affected / exposed	1 / 273 (0.37%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Social circumstances: Other, specify	Additional description: Social circumstances: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders: Other, specify	Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adult respiratory distress syndrome	Additional description: Adult respiratory distress syndrome		

subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	4 / 272 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Aspiration	Additional description: Aspiration		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dyspnea	Additional description: Dyspnea		
subjects affected / exposed	2 / 273 (0.73%)	4 / 273 (1.47%)	2 / 272 (0.74%)
occurrences causally related to treatment / all	0 / 2	1 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm	Additional description: Bronchospasm		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary edema	Additional description: Pulmonary edema		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure	Additional description: Respiratory failure		

subjects affected / exposed	1 / 273 (0.37%)	5 / 273 (1.83%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 4	0 / 0
Psychiatric disorders			
Psychosis	Additional description: Psychosis		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt	Additional description: Suicide attempt		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusion	Additional description: Confusion		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders: Other, specify	Additional description: Psychiatric disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucinations	Additional description: Hallucinations		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations: Other, specify	Additional description: Investigations: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Injury, poisoning and procedural complications: Other, specify	Additional description: Injury, poisoning and procedural complications: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hip fracture	Additional description: Hip fracture		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall	Additional description: Fall		
subjects affected / exposed	2 / 273 (0.73%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial injury	Additional description: Arterial injury		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma	Additional description: Seroma		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture	Additional description: Fracture		
subjects affected / exposed	1 / 273 (0.37%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Ventricular tachycardia	Additional description: Ventricular tachycardia		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain - cardiac	Additional description: Chest pain - cardiac		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Stroke	Additional description: Stroke		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness	Additional description: Depressed level of consciousness		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy	Additional description: Encephalopathy		
subjects affected / exposed	8 / 273 (2.93%)	4 / 273 (1.47%)	4 / 272 (1.47%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 2
Intracranial hemorrhage	Additional description: Intracranial hemorrhage		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope	Additional description: Syncope		
subjects affected / exposed	0 / 273 (0.00%)	3 / 273 (1.10%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders: Other,	Additional description: Nervous system disorders: Other, specify		

specify			
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure	Additional description: Seizure		
subjects affected / exposed	1 / 273 (0.37%)	3 / 273 (1.10%)	2 / 272 (0.74%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anemia	Additional description: Anemia		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemolysis	Additional description: Hemolysis		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites	Additional description: Ascites		
subjects affected / exposed	6 / 273 (2.20%)	8 / 273 (2.93%)	11 / 272 (4.04%)
occurrences causally related to treatment / all	0 / 7	1 / 13	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders: Other, specify	Additional description: Gastrointestinal disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	3 / 272 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colonic perforation	Additional description: Colonic perforation		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal pain	Additional description: Gastrointestinal pain		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pancreatitis	Additional description: Pancreatitis		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences causally related to treatment / all	1 / 1	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	4 / 273 (1.47%)	5 / 273 (1.83%)	4 / 272 (1.47%)
occurrences causally related to treatment / all	0 / 6	1 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Esophageal hemorrhage	Additional description: Esophageal hemorrhage		
subjects affected / exposed	1 / 273 (0.37%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0

Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	3 / 272 (1.10%)
occurrences causally related to treatment / all	1 / 1	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Esophageal varices hemorrhage	Additional description: Esophageal varices hemorrhage		
subjects affected / exposed	5 / 273 (1.83%)	5 / 273 (1.83%)	7 / 272 (2.57%)
occurrences causally related to treatment / all	0 / 7	1 / 5	0 / 7
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 4

Duodenal perforation	Additional description: Duodenal perforation

subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis	Additional description: Enterocolitis		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal hemorrhage	Additional description: Upper gastrointestinal hemorrhage		
subjects affected / exposed	5 / 273 (1.83%)	12 / 273 (4.40%)	9 / 272 (3.31%)
occurrences causally related to treatment / all	0 / 5	2 / 12	1 / 10
deaths causally related to treatment / all	0 / 3	1 / 6	0 / 4
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 273 (0.00%)	3 / 273 (1.10%)	3 / 272 (1.10%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis	Additional description: Colitis		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal hemorrhage	Additional description: Rectal hemorrhage		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal hemorrhage	Additional description: Lower gastrointestinal hemorrhage		
subjects affected / exposed	2 / 273 (0.73%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Colonic obstruction	Additional description: Colonic obstruction		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric hemorrhage	Additional description: Gastric hemorrhage		

subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhea	Additional description: Diarrhea		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	4 / 272 (1.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatobiliary disorders: Other, specify	Additional description: Hepatobiliary disorders: Other, specify		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure	Additional description: Hepatic failure		
subjects affected / exposed	26 / 273 (9.52%)	27 / 273 (9.89%)	23 / 272 (8.46%)
occurrences causally related to treatment / all	0 / 26	0 / 27	1 / 23
deaths causally related to treatment / all	0 / 22	0 / 14	1 / 17
Skin and subcutaneous tissue disorders			
Skin ulceration	Additional description: Skin ulceration		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic epidermal necrolysis	Additional description: Toxic epidermal necrolysis		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal and urinary disorders: Other, specify	Additional description: Renal and urinary disorders: Other, specify		

subjects affected / exposed	1 / 273 (0.37%)	5 / 273 (1.83%)	9 / 272 (3.31%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 9
deaths causally related to treatment / all	0 / 1	0 / 4	0 / 6
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	9 / 273 (3.30%)	5 / 273 (1.83%)	4 / 272 (1.47%)
occurrences causally related to treatment / all	0 / 9	1 / 5	0 / 4
deaths causally related to treatment / all	0 / 3	0 / 3	0 / 1
Musculoskeletal and connective tissue disorders			
Back pain	Additional description: Back pain		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle weakness lower limb	Additional description: Muscle weakness lower limb		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis	Additional description: Myositis		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatic infection	Additional description: Hepatic infection		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Endocarditis infective	Additional description: Endocarditis infective		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection	Additional description: Abdominal infection		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sepsis	Additional description: Sepsis		
subjects affected / exposed	7 / 273 (2.56%)	11 / 273 (4.03%)	6 / 272 (2.21%)
occurrences causally related to treatment / all	1 / 8	3 / 11	2 / 6
deaths causally related to treatment / all	0 / 2	0 / 4	0 / 4
Joint infection	Additional description: Joint infection		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection	Additional description: Skin infection		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations: Other, specify	Additional description: Infections and infestations: Other, specify		
subjects affected / exposed	5 / 273 (1.83%)	8 / 273 (2.93%)	3 / 272 (1.10%)
occurrences causally related to treatment / all	2 / 6	4 / 9	1 / 3
deaths causally related to treatment / all	1 / 3	2 / 3	0 / 1
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection	Additional description: Lung infection		
subjects affected / exposed	11 / 273 (4.03%)	19 / 273 (6.96%)	6 / 272 (2.21%)
occurrences causally related to treatment / all	3 / 11	12 / 20	3 / 6
deaths causally related to treatment / all	2 / 3	5 / 9	0 / 1
Metabolism and nutrition disorders			
Hypoglycemia	Additional description: Hypoglycemia		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycemia	Additional description: Hyperglycemia		
subjects affected / exposed	0 / 273 (0.00%)	3 / 273 (1.10%)	0 / 272 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dehydration	Additional description: Dehydration		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PTX/Pred.		
Total subjects affected by serious adverse events			
subjects affected / exposed	116 / 274 (42.34%)		
number of deaths (all causes)	37		
number of deaths resulting from adverse events	37		
Vascular disorders			
Thromboembolic event	Additional description: Thromboembolic event		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hematoma	Additional description: Hematoma		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Edema limbs	Additional description: Edema limbs		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Multi-organ failure	Additional description: Multi-organ failure		
subjects affected / exposed	7 / 274 (2.55%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 7		
General disorders and administration site conditions: Other, specify	Additional description: General disorders and administration site conditions: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malaise	Additional description: Malaise		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Social circumstances: Other, specify	Additional description: Social circumstances: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders: Other, specify	Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Adult respiratory distress syndrome	Additional description: Adult respiratory distress syndrome		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspiration	Additional description: Aspiration		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnea	Additional description: Dyspnea		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bronchospasm	Additional description: Bronchospasm		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary edema	Additional description: Pulmonary edema		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure	Additional description: Respiratory failure		
subjects affected / exposed	5 / 274 (1.82%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	1 / 2		
Psychiatric disorders			
Psychosis	Additional description: Psychosis		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt	Additional description: Suicide attempt		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Confusion	Additional description: Confusion		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders: Other, specify	Additional description: Psychiatric disorders: Other, specify		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hallucinations	Additional description: Hallucinations		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations: Other, specify	Additional description: Investigations: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications: Other, specify	Additional description: Injury, poisoning and procedural complications: Other, specify		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hip fracture	Additional description: Hip fracture		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall	Additional description: Fall		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Arterial injury	Additional description: Arterial injury		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Seroma	Additional description: Seroma		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fracture	Additional description: Fracture		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Ventricular tachycardia	Additional description: Ventricular tachycardia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest pain - cardiac	Additional description: Chest pain - cardiac		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Stroke	Additional description: Stroke		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Depressed level of consciousness	Additional description: Depressed level of consciousness		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalopathy	Additional description: Encephalopathy		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Intracranial hemorrhage	Additional description: Intracranial hemorrhage		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope	Additional description: Syncope		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders: Other, specify	Additional description: Nervous system disorders: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure	Additional description: Seizure		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anemia	Additional description: Anemia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hemolysis	Additional description: Hemolysis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ascites	Additional description: Ascites		
subjects affected / exposed	13 / 274 (4.74%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders: Other, specify	Additional description: Gastrointestinal disorders: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colonic perforation	Additional description: Colonic perforation		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal pain	Additional description: Gastrointestinal pain		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis	Additional description: Pancreatitis		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	1 / 1		
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Esophageal hemorrhage	Additional description: Esophageal hemorrhage		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Esophageal varices hemorrhage	Additional description: Esophageal varices hemorrhage		
subjects affected / exposed	5 / 274 (1.82%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Duodenal perforation	Additional description: Duodenal perforation		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis	Additional description: Enterocolitis		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal hemorrhage	Additional description: Upper gastrointestinal hemorrhage		
subjects affected / exposed	13 / 274 (4.74%)		
occurrences causally related to treatment / all	3 / 18		
deaths causally related to treatment / all	0 / 1		
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis	Additional description: Colitis		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal hemorrhage	Additional description: Rectal hemorrhage		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal hemorrhage	Additional description: Lower gastrointestinal hemorrhage		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colonic obstruction	Additional description: Colonic obstruction		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastric hemorrhage	Additional description: Gastric hemorrhage		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhea	Additional description: Diarrhea		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatobiliary disorders: Other, specify	Additional description: Hepatobiliary disorders: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic failure	Additional description: Hepatic failure		

subjects affected / exposed	21 / 274 (7.66%)		
occurrences causally related to treatment / all	1 / 22		
deaths causally related to treatment / all	0 / 12		
Skin and subcutaneous tissue disorders			
Skin ulceration	Additional description: Skin ulceration		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic epidermal necrolysis	Additional description: Toxic epidermal necrolysis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal and urinary disorders: Other, specify	Additional description: Renal and urinary disorders: Other, specify		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	5 / 274 (1.82%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
Musculoskeletal and connective tissue disorders			
Back pain	Additional description: Back pain		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscle weakness lower limb	Additional description: Muscle weakness lower limb		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myositis	Additional description: Myositis		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Hepatic infection	Additional description: Hepatic infection		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Endocarditis infective	Additional description: Endocarditis infective		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal infection	Additional description: Abdominal infection		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis	Additional description: Sepsis		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Joint infection	Additional description: Joint infection		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin infection	Additional description: Skin infection		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations: Other, specify	Additional description: Infections and infestations: Other, specify		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection	Additional description: Urinary tract infection		

subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection	Additional description: Lung infection		
subjects affected / exposed	18 / 274 (6.57%)		
occurrences causally related to treatment / all	4 / 18		
deaths causally related to treatment / all	1 / 7		
Metabolism and nutrition disorders			
Hypoglycemia	Additional description: Hypoglycemia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycemia	Additional description: Hyperglycemia		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration	Additional description: Dehydration		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo/Placebo	Placebo/Pred.	PTX/Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 273 (38.83%)	96 / 273 (35.16%)	102 / 272 (37.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (inc cysts and polyps): Other, specify	Additional description: Neoplasms benign, malignant and unspecified (inc cysts and polyps): Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify	Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify		

subjects affected / exposed	2 / 273 (0.73%)	3 / 273 (1.10%)	1 / 272 (0.37%)
occurrences (all)	2	3	1
Vascular disorders			
Peripheral ischemia	Additional description: Peripheral ischemia		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	2	0	0
Vascular disorders : Other, specify	Additional description: Vascular disorders : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Hematoma	Additional description: Hematoma		
subjects affected / exposed	1 / 273 (0.37%)	3 / 273 (1.10%)	1 / 272 (0.37%)
occurrences (all)	1	3	1
Hypotension	Additional description: Hypotension		
subjects affected / exposed	4 / 273 (1.47%)	1 / 273 (0.37%)	3 / 272 (1.10%)
occurrences (all)	4	1	3
Thromboembolic event	Additional description: Thromboembolic event		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	1	1	1
General disorders and administration site conditions			
Fever	Additional description: Fever		
subjects affected / exposed	5 / 273 (1.83%)	6 / 273 (2.20%)	6 / 272 (2.21%)
occurrences (all)	6	6	6
General disorders and administration site conditions: Other, specify	Additional description: General disorders and administration site conditions: Other, specify		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	1	0	2
Fatigue	Additional description: Fatigue		
subjects affected / exposed	3 / 273 (1.10%)	1 / 273 (0.37%)	4 / 272 (1.47%)
occurrences (all)	3	1	4
Localised edema	Additional description: Localised edema		
subjects affected / exposed	11 / 273 (4.03%)	5 / 273 (1.83%)	3 / 272 (1.10%)
occurrences (all)	15	6	3
Hypothermia	Additional description: Hypothermia		
subjects affected / exposed	2 / 273 (0.73%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	2	1	0
Injection site reaction	Additional description: Injection site reaction		

subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Edema limbs	Additional description: Edema limbs		
subjects affected / exposed	5 / 273 (1.83%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	5	1	0
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Skin infection	Additional description: Skin infection		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Malaise	Additional description: Malaise		
subjects affected / exposed	1 / 273 (0.37%)	2 / 273 (0.73%)	6 / 272 (2.21%)
occurrences (all)	1	2	6
Facial pain	Additional description: Facial pain		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Pruritus	Additional description: Pruritus		
subjects affected / exposed	4 / 273 (1.47%)	3 / 273 (1.10%)	5 / 272 (1.84%)
occurrences (all)	4	3	5
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	3 / 273 (1.10%)	2 / 273 (0.73%)	5 / 272 (1.84%)
occurrences (all)	3	2	5
Reproductive system and breast disorders			
Vaginal hemorrhage	Additional description: Vaginal hemorrhage		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Erectile dysfunction	Additional description: Erectile dysfunction		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Gynecomastia	Additional description: Gynecomastia		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Reproductive system and breast disorders: Other, specify	Additional description: Reproductive system and breast disorders: Other, specify		

subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Reporoductive system and breast disorders : Other, specify	Additional description: Reporoductive system and breast disorders : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	6 / 273 (2.20%)	2 / 273 (0.73%)	1 / 272 (0.37%)
occurrences (all)	6	2	1
Pleuritic pain	Additional description: Pleuritic pain		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Sore throat	Additional description: Sore throat		
subjects affected / exposed	3 / 273 (1.10%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	3	1	0
Pulmonary edema	Additional description: Pulmonary edema		
subjects affected / exposed	2 / 273 (0.73%)	2 / 273 (0.73%)	2 / 272 (0.74%)
occurrences (all)	2	2	2
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences (all)	0	1	2
Dyspnea	Additional description: Dyspnea		
subjects affected / exposed	4 / 273 (1.47%)	8 / 273 (2.93%)	2 / 272 (0.74%)
occurrences (all)	4	8	2
Respiratory, thoracic and mediastinal disorders: Other, specify	Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	1	0	2
Pharyngolarygeal pain	Additional description: Pharyngolarygeal pain		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Epistaxis	Additional description: Epistaxis		

subjects affected / exposed	3 / 273 (1.10%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences (all)	3	1	2
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	1	0	1
Productive cough	Additional description: Productive cough		
subjects affected / exposed	2 / 273 (0.73%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	2	1	0
Cough	Additional description: Cough		
subjects affected / exposed	1 / 273 (0.37%)	2 / 273 (0.73%)	1 / 272 (0.37%)
occurrences (all)	1	2	1
Bronchospasm	Additional description: Bronchospasm		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation	Additional description: Agitation		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	0	1	1
Libido decreased	Additional description: Libido decreased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders : Other, specify	Additional description: Psychiatric disorders : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Psychosis	Additional description: Psychosis		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Hallucinations	Additional description: Hallucinations		
subjects affected / exposed	4 / 273 (1.47%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	4	1	1
Depression	Additional description: Depression		
subjects affected / exposed	3 / 273 (1.10%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	3	0	0
Confusion	Additional description: Confusion		
subjects affected / exposed	3 / 273 (1.10%)	1 / 273 (0.37%)	3 / 272 (1.10%)
occurrences (all)	3	1	3

Suicide attempt	Additional description: Suicide attempt		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	1	0	1
Insomnia	Additional description: Insomnia		
subjects affected / exposed	3 / 273 (1.10%)	3 / 273 (1.10%)	1 / 272 (0.37%)
occurrences (all)	3	3	1
Investigations			
Alanine aminotranferase increased	Additional description: Alanine aminotranferase increased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Weight gain	Additional description: Weight gain		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
INR increased	Additional description: INR increased		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	1	0	1
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Alkaline phosphatase increased	Additional description: Alkaline phosphatase increased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	0	0	2
White blood cell decreased	Additional description: White blood cell decreased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	0	0	2
Lymphocyte count increased	Additional description: Lymphocyte count increased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	0 / 273 (0.00%)	5 / 273 (1.83%)	4 / 272 (1.47%)
occurrences (all)	0	5	4
Weight loss	Additional description: Weight loss		

subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Hypokalemia	Additional description: Hypokalemia		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Alanine transferase increased	Additional description: Alanine transferase increased		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	1	0	2
Cardiac troponin T increased	Additional description: Cardiac troponin T increased		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Investigations: Other, specify	Additional description: Investigations: Other, specify		
subjects affected / exposed	2 / 273 (0.73%)	2 / 273 (0.73%)	3 / 272 (1.10%)
occurrences (all)	2	2	3
Serum amylase increased	Additional description: Serum amylase increased		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences (all)	0	2	0
Creatinine increased	Additional description: Creatinine increased		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
Spinal fracture	Additional description: Spinal fracture		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Fall	Additional description: Fall		
subjects affected / exposed	8 / 273 (2.93%)	7 / 273 (2.56%)	8 / 272 (2.94%)
occurrences (all)	10	8	12
Wound complication	Additional description: Wound complication		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Fracture	Additional description: Fracture		

subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Injury to jugular vein	Additional description: Injury to jugular vein		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications: Other, specify	Additional description: Injury, poisoning and procedural complications: Other, specify		
subjects affected / exposed	3 / 273 (1.10%)	2 / 273 (0.73%)	3 / 272 (1.10%)
occurrences (all)	3	2	3
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Bruising	Additional description: Bruising		
subjects affected / exposed	3 / 273 (1.10%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	3	2	0
Cardiac disorders			
Palpitations	Additional description: Palpitations		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	1 / 273 (0.37%)	3 / 273 (1.10%)	1 / 272 (0.37%)
occurrences (all)	1	3	1
Left ventricular systolic dysfunction	Additional description: Left ventricular systolic dysfunction		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Cardiac disorders : Other, specify	Additional description: Cardiac disorders : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia	Additional description: Sinus tachycardia		

subjects affected / exposed	3 / 273 (1.10%)	2 / 273 (0.73%)	3 / 272 (1.10%)
occurrences (all)	3	2	4
Chest pain - cardiac	Additional description: Chest pain - cardiac		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	2	0
Acute coronary syndrome	Additional description: Acute coronary syndrome		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders: Other, specify	Additional description: Cardiac disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Nervous system disorders			
Depressed level of consiousness	Additional description: Depressed level of consiousness		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	4 / 272 (1.47%)
occurrences (all)	1	0	4
Syncope	Additional description: Syncope		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	0	1	1
Seizure	Additional description: Seizure		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	1	0	1
Tremor	Additional description: Tremor		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders: Other, specify	Additional description: Nervous system disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Psychiatric disorders: Other, specify	Additional description: Psychiatric disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Encephalopathy	Additional description: Encephalopathy		

subjects affected / exposed	3 / 273 (1.10%)	4 / 273 (1.47%)	3 / 272 (1.10%)
occurrences (all)	3	5	3
Dizziness	Additional description: Dizziness		
subjects affected / exposed	3 / 273 (1.10%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences (all)	3	2	0
Headache	Additional description: Headache		
subjects affected / exposed	2 / 273 (0.73%)	5 / 273 (1.83%)	4 / 272 (1.47%)
occurrences (all)	2	6	4
Dysphasia	Additional description: Dysphasia		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	4 / 273 (1.47%)	2 / 273 (0.73%)	3 / 272 (1.10%)
occurrences (all)	4	4	3
Blood and lymphatic system disorder : Other, specify	Additional description: Blood and lymphatic system disorder : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	0	0	2
Anemia	Additional description: Anemia		
subjects affected / exposed	2 / 273 (0.73%)	2 / 273 (0.73%)	5 / 272 (1.84%)
occurrences (all)	2	2	6
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Blurred vision	Additional description: Blurred vision		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Eye infection	Additional description: Eye infection		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Esophagitis	Additional description: Esophagitis		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0

Nausea	Additional description: Nausea		
subjects affected / exposed	6 / 273 (2.20%)	1 / 273 (0.37%)	19 / 272 (6.99%)
occurrences (all)	6	1	19
Bloating	Additional description: Bloating		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Oral hemorrhage	Additional description: Oral hemorrhage		
subjects affected / exposed	1 / 273 (0.37%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders: Other, specify	Additional description: Gastrointestinal disorders: Other, specify		
subjects affected / exposed	3 / 273 (1.10%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	3	0	1
Diarrhea	Additional description: Diarrhea		
subjects affected / exposed	12 / 273 (4.40%)	5 / 273 (1.83%)	19 / 272 (6.99%)
occurrences (all)	12	5	22
Esophageal varices hemorrhage	Additional description: Esophageal varices hemorrhage		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	1	0	2
Gastritis	Additional description: Gastritis		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications: Other, specify	Additional description: Injury, poisoning and procedural complications: Other, specify		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify	Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Hemorrhoids	Additional description: Hemorrhoids		
subjects affected / exposed	2 / 273 (0.73%)	2 / 273 (0.73%)	1 / 272 (0.37%)
occurrences (all)	2	2	1
Duodenal ulcer	Additional description: Duodenal ulcer		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	1	1	0
Haemorrhoidal haemorrhage	Additional description: Haemorrhoidal haemorrhage		

subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Rectal hemorrhage	Additional description: Rectal hemorrhage		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	2	0	2
Upper gastrointestinal hemorrhage	Additional description: Upper gastrointestinal hemorrhage		
subjects affected / exposed	7 / 273 (2.56%)	7 / 273 (2.56%)	1 / 272 (0.37%)
occurrences (all)	7	7	1
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	1	1	0
Rectal pain	Additional description: Rectal pain		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Gastric ulcer	Additional description: Gastric ulcer		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	14 / 273 (5.13%)	8 / 273 (2.93%)	11 / 272 (4.04%)
occurrences (all)	15	11	12
Dental caries	Additional description: Dental caries		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	9 / 273 (3.30%)	5 / 273 (1.83%)	13 / 272 (4.78%)
occurrences (all)	11	5	16
Enterocolitis infectious	Additional description: Enterocolitis infectious		
subjects affected / exposed	1 / 273 (0.37%)	3 / 273 (1.10%)	1 / 272 (0.37%)
occurrences (all)	1	3	1
Esophageal perforation	Additional description: Esophageal perforation		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	0	1	1
Esophageal ulcer	Additional description: Esophageal ulcer		

subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Esophageal infection	Additional description: Esophageal infection		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Ascites	Additional description: Ascites		
subjects affected / exposed	10 / 273 (3.66%)	10 / 273 (3.66%)	10 / 272 (3.68%)
occurrences (all)	16	11	12
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	4 / 273 (1.47%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	4	0	1
Gastroesophageal reflux disease	Additional description: Gastroesophageal reflux disease		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	2 / 273 (0.73%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences (all)	2	1	2
Rectal stenosis	Additional description: Rectal stenosis		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Mucositis oral	Additional description: Mucositis oral		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Lower gastrointestinal hemorrhage	Additional description: Lower gastrointestinal hemorrhage		
subjects affected / exposed	5 / 273 (1.83%)	6 / 273 (2.20%)	3 / 272 (1.10%)
occurrences (all)	5	6	3
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 273 (0.00%)	4 / 273 (1.47%)	2 / 272 (0.74%)
occurrences (all)	0	4	2
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hepatic failure	Additional description: Hepatic failure		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences (all)	0	2	0

Hepatobiliary disorders: Other, specify	Additional description: Hepatobiliary disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Biliary tract infection	Additional description: Biliary tract infection		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Portal hypertension	Additional description: Portal hypertension		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	6 / 273 (2.20%)	4 / 273 (1.47%)	7 / 272 (2.57%)
occurrences (all)	6	4	9
Skin and subcutaneous tissue disorder : Other, specify	Additional description: Skin and subcutaneous tissue disorder : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	2 / 272 (0.74%)
occurrences (all)	0	2	2
Pruritus	Additional description: Pruritus		
subjects affected / exposed	7 / 273 (2.56%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	7	0	0
Alopecia	Additional description: Alopecia		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Papulopustular rash	Additional description: Papulopustular rash		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders: Other, specify	Additional description: Skin and subcutaneous tissue disorders: Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Erythema multiforme	Additional description: Erythema multiforme		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Skin ulceration	Additional description: Skin ulceration		

subjects affected / exposed	2 / 273 (0.73%)	2 / 273 (0.73%)	1 / 272 (0.37%)
occurrences (all)	2	2	1
Skin infection	Additional description: Skin infection		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Renal and urinary disorders: Other, specify	Additional description: Renal and urinary disorders: Other, specify		
subjects affected / exposed	2 / 273 (0.73%)	2 / 273 (0.73%)	2 / 272 (0.74%)
occurrences (all)	2	2	2
Hematuria	Additional description: Hematuria		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	1	0	2
Haematuria	Additional description: Haematuria		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Chronic kidney disease	Additional description: Chronic kidney disease		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Urinary tract pain	Additional description: Urinary tract pain		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	1	0	1
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Urinary tract obstruction	Additional description: Urinary tract obstruction		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	5 / 273 (1.83%)	0 / 273 (0.00%)	4 / 272 (1.47%)
occurrences (all)	6	0	4
Endocrine disorders			
Endocrine disorders : Other, specify	Additional description: Endocrine disorders : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Hypothyroidism	Additional description: Hypothyroidism		

subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Chest wall pain	Additional description: Chest wall pain		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	0	0	0
Arthraligia	Additional description: Arthraligia		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	2	0	1
Back pain	Additional description: Back pain		
subjects affected / exposed	6 / 273 (2.20%)	2 / 273 (0.73%)	2 / 272 (0.74%)
occurrences (all)	6	2	2
Flank pain	Additional description: Flank pain		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorder : Other, specify	Additional description: Musculoskeletal and connective tissue disorder : Other, specify		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Osteoporosis	Additional description: Osteoporosis		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Generalised muscle weakness	Additional description: Generalised muscle weakness		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Fracture	Additional description: Fracture		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	3 / 273 (1.10%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	3	1	1
Myalgia	Additional description: Myalgia		

subjects affected / exposed	6 / 273 (2.20%)	2 / 273 (0.73%)	4 / 272 (1.47%)
occurrences (all)	6	2	5
Infections and infestations			
Vaginal infection	Additional description: Vaginal infection		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
Hepatitis viral	Additional description: Hepatitis viral		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	0	1	1
Sepsis	Additional description: Sepsis		
subjects affected / exposed	3 / 273 (1.10%)	10 / 273 (3.66%)	4 / 272 (1.47%)
occurrences (all)	3	13	6
Wound infection	Additional description: Wound infection		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Mucosal infection	Additional description: Mucosal infection		
subjects affected / exposed	3 / 273 (1.10%)	0 / 273 (0.00%)	2 / 272 (0.74%)
occurrences (all)	3	0	2
Lung infection	Additional description: Lung infection		
subjects affected / exposed	9 / 273 (3.30%)	10 / 273 (3.66%)	8 / 272 (2.94%)
occurrences (all)	9	12	8
Esophageal infection	Additional description: Esophageal infection		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Rash pustular	Additional description: Rash pustular		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	11 / 273 (4.03%)	9 / 273 (3.30%)	7 / 272 (2.57%)
occurrences (all)	12	9	7
Skin infection	Additional description: Skin infection		
subjects affected / exposed	3 / 273 (1.10%)	6 / 273 (2.20%)	2 / 272 (0.74%)
occurrences (all)	3	6	2
Infections and infestations: Other, specify	Additional description: Infections and infestations: Other, specify		

subjects affected / exposed	4 / 273 (1.47%)	1 / 273 (0.37%)	4 / 272 (1.47%)
occurrences (all)	5	1	4
Phlebitis infective	Additional description: Phlebitis infective		
subjects affected / exposed	0 / 273 (0.00%)	2 / 273 (0.73%)	0 / 272 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Hypernatremia	Additional description: Hypernatremia		
subjects affected / exposed	0 / 273 (0.00%)	1 / 273 (0.37%)	0 / 272 (0.00%)
occurrences (all)	0	1	0
White blood cell decreased	Additional description: White blood cell decreased		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Dehydration	Additional description: Dehydration		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	0	0	1
Hyperglycemia	Additional description: Hyperglycemia		
subjects affected / exposed	1 / 273 (0.37%)	2 / 273 (0.73%)	2 / 272 (0.74%)
occurrences (all)	1	2	2
Anorexia	Additional description: Anorexia		
subjects affected / exposed	1 / 273 (0.37%)	1 / 273 (0.37%)	1 / 272 (0.37%)
occurrences (all)	1	1	1
Metabolism and nutrition disorders : Other, specify	Additional description: Metabolism and nutrition disorders : Other, specify		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	2	0	1
Hypomagnesemia	Additional description: Hypomagnesemia		
subjects affected / exposed	2 / 273 (0.73%)	0 / 273 (0.00%)	0 / 272 (0.00%)
occurrences (all)	3	0	0
Hyponatremia	Additional description: Hyponatremia		
subjects affected / exposed	2 / 273 (0.73%)	3 / 273 (1.10%)	4 / 272 (1.47%)
occurrences (all)	2	4	5
Hypoalbuminemia	Additional description: Hypoalbuminemia		
subjects affected / exposed	2 / 273 (0.73%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences (all)	2	1	2
Hypophosphatemia	Additional description: Hypophosphatemia		

subjects affected / exposed	2 / 273 (0.73%)	1 / 273 (0.37%)	2 / 272 (0.74%)
occurrences (all)	2	1	2
Hypocalcemia	Additional description: Hypocalcemia		
subjects affected / exposed	0 / 273 (0.00%)	0 / 273 (0.00%)	3 / 272 (1.10%)
occurrences (all)	0	0	4
Hypokalemia	Additional description: Hypokalemia		
subjects affected / exposed	7 / 273 (2.56%)	8 / 273 (2.93%)	1 / 272 (0.37%)
occurrences (all)	8	9	1
Hyperkalemia	Additional description: Hyperkalemia		
subjects affected / exposed	1 / 273 (0.37%)	0 / 273 (0.00%)	1 / 272 (0.37%)
occurrences (all)	1	0	1

Non-serious adverse events	PTX/Pred.		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	91 / 274 (33.21%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (inc cysts and polyps): Other, specify	Additional description: Neoplasms benign, malignant and unspecified (inc cysts and polyps): Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify	Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Vascular disorders			
Peripheral ischemia	Additional description: Peripheral ischemia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Vascular disorders : Other, specify	Additional description: Vascular disorders : Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Hematoma	Additional description: Hematoma		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Hypotension	Additional description: Hypotension		

subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Thromboembolic event	Additional description: Thromboembolic event		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fever	Additional description: Fever		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	4		
General disorders and administration site conditions: Other, specify	Additional description: General disorders and administration site conditions: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Fatigue	Additional description: Fatigue		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	4		
Localised edema	Additional description: Localised edema		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	4		
Hypothermia	Additional description: Hypothermia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Injection site reaction	Additional description: Injection site reaction		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Edema limbs	Additional description: Edema limbs		
subjects affected / exposed	7 / 274 (2.55%)		
occurrences (all)	7		
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Skin infection	Additional description: Skin infection		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Malaise	Additional description: Malaise		

subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Facial pain	Additional description: Facial pain		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Pruritus	Additional description: Pruritus		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Vaginal hemorrhage	Additional description: Vaginal hemorrhage		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Erectile dysfunction	Additional description: Erectile dysfunction		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Gynecomastia	Additional description: Gynecomastia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders: Other, specify	Additional description: Reproductive system and breast disorders: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Reporoductive system and breast disorders : Other, specify	Additional description: Reporoductive system and breast disorders : Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Pleuritic pain	Additional description: Pleuritic pain		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		

Sore throat	Additional description: Sore throat		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Pulmonary edema	Additional description: Pulmonary edema		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Hypoxia	Additional description: Hypoxia		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Dyspnea	Additional description: Dyspnea		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders: Other, specify	Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Pharyngolarygeal pain	Additional description: Pharyngolarygeal pain		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Productive cough	Additional description: Productive cough		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Cough	Additional description: Cough		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Bronchospasm	Additional description: Bronchospasm		

subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation	Additional description: Agitation		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Libido decreased	Additional description: Libido decreased		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Psychiatric disorders : Other, specify	Additional description: Psychiatric disorders : Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Psychosis	Additional description: Psychosis		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	2		
Hallucinations	Additional description: Hallucinations		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Depression	Additional description: Depression		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Confusion	Additional description: Confusion		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Suicide attempt	Additional description: Suicide attempt		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Insomnia	Additional description: Insomnia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotranferase increased	Additional description: Alanine aminotranferase increased		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Weight gain	Additional description: Weight gain		

subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
INR increased	Additional description: INR increased		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Alkaline phosphatase increased	Additional description: Alkaline phosphatase increased		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
White blood cell decreased	Additional description: White blood cell decreased		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Lymphocyte count increased	Additional description: Lymphocyte count increased		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	6 / 274 (2.19%)		
occurrences (all)	6		
Weight loss	Additional description: Weight loss		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Hypokalemia	Additional description: Hypokalemia		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Alanine transferase increased	Additional description: Alanine transferase increased		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		

Cardiac troponin T increased	Additional description: Cardiac troponin T increased		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Investigations: Other, specify	Additional description: Investigations: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Serum amylase increased	Additional description: Serum amylase increased		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Creatinine increased	Additional description: Creatinine increased		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Spinal fracture	Additional description: Spinal fracture		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Fall	Additional description: Fall		
subjects affected / exposed	7 / 274 (2.55%)		
occurrences (all)	8		
Wound complication	Additional description: Wound complication		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Fracture	Additional description: Fracture		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Injury to jugular vein	Additional description: Injury to jugular vein		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications: Other, specify	Additional description: Injury, poisoning and procedural complications: Other, specify		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Sepsis	Additional description: Sepsis		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Bruising	Additional description: Bruising		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations	Additional description: Palpitations		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Left ventricular systolic dysfunction	Additional description: Left ventricular systolic dysfunction		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Cardiac disorders : Other, specify	Additional description: Cardiac disorders : Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Sinus tachycardia	Additional description: Sinus tachycardia		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Chest pain - cardiac	Additional description: Chest pain - cardiac		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Supraventricular tachycardia	Additional description: Supraventricular tachycardia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Acute coronary syndrome	Additional description: Acute coronary syndrome		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Cardiac disorders: Other, specify	Additional description: Cardiac disorders: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		

Nervous system disorders			
Depressed level of consiousness	Additional description: Depressed level of consiousness		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Syncope	Additional description: Syncope		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Seizure	Additional description: Seizure		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Tremor	Additional description: Tremor		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Nervous system disorders: Other, specify	Additional description: Nervous system disorders: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Psychiatric disorders: Other, specify	Additional description: Psychiatric disorders: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Encephalopathy	Additional description: Encephalopathy		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	5		
Dizziness	Additional description: Dizziness		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	4		
Headache	Additional description: Headache		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Dysphasia	Additional description: Dysphasia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Leukocytosis	Additional description: Leukocytosis		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Blood and lymphatic system disorder : Other, specify	Additional description: Blood and lymphatic system disorder : Other, specify		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Anemia	Additional description: Anemia		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Eye disorders			
Blurred vision	Additional description: Blurred vision		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Eye infection	Additional description: Eye infection		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Esophagitis	Additional description: Esophagitis		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Nausea	Additional description: Nausea		
subjects affected / exposed	8 / 274 (2.92%)		
occurrences (all)	8		
Bloating	Additional description: Bloating		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Oral hemorrhage	Additional description: Oral hemorrhage		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders: Other, specify	Additional description: Gastrointestinal disorders: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Diarrhea	Additional description: Diarrhea		
subjects affected / exposed	8 / 274 (2.92%)		
occurrences (all)	9		
Esophageal varices hemorrhage	Additional description: Esophageal varices hemorrhage		

subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	4		
Gastritis	Additional description: Gastritis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications: Other, specify	Additional description: Injury, poisoning and procedural complications: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify	Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Hemorrhoids	Additional description: Hemorrhoids		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Duodenal ulcer	Additional description: Duodenal ulcer		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Haemorrhoidal haemorrhage	Additional description: Haemorrhoidal haemorrhage		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Rectal hemorrhage	Additional description: Rectal hemorrhage		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Upper gastrointestinal hemorrhage	Additional description: Upper gastrointestinal hemorrhage		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	6		
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Rectal pain	Additional description: Rectal pain		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Gastric ulcer	Additional description: Gastric ulcer		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	6 / 274 (2.19%)		
occurrences (all)	8		
Dental caries	Additional description: Dental caries		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	11 / 274 (4.01%)		
occurrences (all)	12		
Enterocolitis infectious	Additional description: Enterocolitis infectious		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Esophageal perforation	Additional description: Esophageal perforation		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Esophageal ulcer	Additional description: Esophageal ulcer		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Esophageal infection	Additional description: Esophageal infection		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Ascites	Additional description: Ascites		
subjects affected / exposed	11 / 274 (4.01%)		
occurrences (all)	14		
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Gastroesophageal reflux disease	Additional description: Gastroesophageal reflux disease		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Abdominal distension	Additional description: Abdominal distension		

subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Rectal stenosis	Additional description: Rectal stenosis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Mucositis oral	Additional description: Mucositis oral		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Lower gastrointestinal hemorrhage	Additional description: Lower gastrointestinal hemorrhage		
subjects affected / exposed	7 / 274 (2.55%)		
occurrences (all)	8		
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Hepatobiliary disorders			
Hepatic failure	Additional description: Hepatic failure		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Hepatobiliary disorders: Other, specify	Additional description: Hepatobiliary disorders: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Biliary tract infection	Additional description: Biliary tract infection		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Portal hypertension	Additional description: Portal hypertension		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Rash maculo-papular	Additional description: Rash maculo-papular		

subjects affected / exposed	8 / 274 (2.92%)		
occurrences (all)	9		
Skin and subcutaneous tissue disorder : Other, specify	Additional description: Skin and subcutaneous tissue disorder : Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Pruritus	Additional description: Pruritus		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Alopecia	Additional description: Alopecia		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Papulopustular rash	Additional description: Papulopustular rash		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders: Other, specify	Additional description: Skin and subcutaneous tissue disorders: Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Erythema multiforme	Additional description: Erythema multiforme		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Skin ulceration	Additional description: Skin ulceration		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Skin infection	Additional description: Skin infection		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Renal and urinary disorders			
Renal and urinary disorders: Other, specify	Additional description: Renal and urinary disorders: Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Hematuria	Additional description: Hematuria		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Haematuria	Additional description: Haematuria		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Chronic kidney disease	Additional description: Chronic kidney disease		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Urinary tract pain	Additional description: Urinary tract pain		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Urinary tract obstruction	Additional description: Urinary tract obstruction		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Endocrine disorders			
Endocrine disorders : Other, specify	Additional description: Endocrine disorders : Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Hypothyroidism	Additional description: Hypothyroidism		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Chest wall pain	Additional description: Chest wall pain		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Arthraligia	Additional description: Arthraligia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Back pain	Additional description: Back pain		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Flank pain	Additional description: Flank pain		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorder : Other, specify	Additional description: Musculoskeletal and connective tissue disorder : Other, specify		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Osteoporosis	Additional description: Osteoporosis		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Generalised muscle weakness	Additional description: Generalised muscle weakness		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Fracture	Additional description: Fracture		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Myalgia	Additional description: Myalgia		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Infections and infestations			
Vaginal infection	Additional description: Vaginal infection		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Hepatitis viral	Additional description: Hepatitis viral		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Sepsis	Additional description: Sepsis		
subjects affected / exposed	7 / 274 (2.55%)		
occurrences (all)	8		
Wound infection	Additional description: Wound infection		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Mucosal infection	Additional description: Mucosal infection		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Lung infection	Additional description: Lung infection		
subjects affected / exposed	13 / 274 (4.74%)		
occurrences (all)	15		
Esophageal infection	Additional description: Esophageal infection		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Rash pustular	Additional description: Rash pustular		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	5		
Skin infection	Additional description: Skin infection		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	4		
Infections and infestations: Other, specify	Additional description: Infections and infestations: Other, specify		
subjects affected / exposed	5 / 274 (1.82%)		
occurrences (all)	5		
Phlebitis infective	Additional description: Phlebitis infective		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypernatremia	Additional description: Hypernatremia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
White blood cell decreased	Additional description: White blood cell decreased		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Dehydration	Additional description: Dehydration		

subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Hyperglycemia	Additional description: Hyperglycemia		
subjects affected / exposed	1 / 274 (0.36%)		
occurrences (all)	1		
Anorexia	Additional description: Anorexia		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Metabolism and nutrition disorders : Other, specify	Additional description: Metabolism and nutrition disorders : Other, specify		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Hypomagnesemia	Additional description: Hypomagnesemia		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Hyponatremia	Additional description: Hyponatremia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	0		
Hypoalbuminemia	Additional description: Hypoalbuminemia		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	2		
Hypophosphatemia	Additional description: Hypophosphatemia		
subjects affected / exposed	3 / 274 (1.09%)		
occurrences (all)	3		
Hypocalcemia	Additional description: Hypocalcemia		
subjects affected / exposed	2 / 274 (0.73%)		
occurrences (all)	3		
Hypokalemia	Additional description: Hypokalemia		
subjects affected / exposed	4 / 274 (1.46%)		
occurrences (all)	4		
Hyperkalemia	Additional description: Hyperkalemia		
subjects affected / exposed	0 / 274 (0.00%)		
occurrences (all)	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/25901427

http://www.ncbi.nlm.nih.gov/pubmed/26691209