



Clinical trial results:

A Phase III Randomised Double-blind Study Comparing Sorafenib With Placebo In Patients With Resected Primary Renal Cell Carcinoma at High or Intermediate Risk of Relapse

Summary

EudraCT number	2006-006079-19
Trial protocol	GB DK BE FR ES
Global end of trial date	10 March 2020

Results information

Result version number	v1 (current)
This version publication date	19 March 2021
First version publication date	19 March 2021

Trial information

Trial identification

Sponsor protocol code	RE05
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Additional study identifiers

ISRCTN number	ISRCTN38934710
ClinicalTrials.gov id (NCT number)	NCT00492258
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical Research Council
Sponsor organisation address	58 Victoria Embankment, London, United Kingdom, EC4Y 0DS
Public contact	Angela Meade, MRC Clinical Trials Unit at UCL, a.meade@ucl.ac.uk
Scientific contact	Angela Meade, MRC Clinical Trials Unit at UCL, a.meade@ucl.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	13 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 June 2019
Global end of trial reached?	Yes
Global end of trial date	10 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The standard treatment for patients with a kidney cancer which has not spread to other organs is to remove all or part of the diseased kidney (nephrectomy). The standard policy after this is watchful waiting. This means no treatment, but having regular checks so that if the cancer does come back it is caught early.

The principal research question is whether sorafenib increases disease free survival (DFS) i.e reduces the risk of kidney cancer returning.

Protection of trial subjects:

Not applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 July 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 19
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	United Kingdom: 1331
Country: Number of subjects enrolled	Belgium: 36
Country: Number of subjects enrolled	Denmark: 20
Country: Number of subjects enrolled	France: 122
Country: Number of subjects enrolled	Australia: 168
Worldwide total number of subjects	1711
EEA total number of subjects	1543

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)	1195
From 65 to 84 years	515
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	1711
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Number of subjects completed	1711
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Period 1

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

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description: -

Arm type	Placebo
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Investigational medicinal product name	Placebo
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

Oral administration twice daily, matching active drug.

Arm title	1 Year Sorafenib + 2 Placebo
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Sorafenib
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

400mg oral administration twice daily. Dose reductions were permitted in the event of significant toxicity. Subsequent re-escalation was allowed but not mandatory.

Arm title	3 Years Sorafenib
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Sorafenib
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

400 mg oral tablet, twice daily. Dose reductions were permitted in the event of significant toxicity. Subsequent re-escalation was allowed but not mandatory

Number of subjects in period 1	Placebo	1 Year Sorafenib + 2 Placebo	3 Years Sorafenib
Started	430	642	639
Completed	430	642	639

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	1 Year Sorafenib + 2 Placebo
Reporting group description: -	
Reporting group title	3 Years Sorafenib
Reporting group description: -	

Reporting group values	Placebo	1 Year Sorafenib + 2 Placebo	3 Years Sorafenib
Number of subjects	430	642	639
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	301	440	454
From 65-84 years	129	201	185
85 years and over	0	1	0
Age continuous Units: years			
arithmetic mean	58.4	58.3	58.0
standard deviation	± 10.3	± 10.6	± 10.9
Gender categorical Units: Subjects			
Female	124	190	181
Male	306	452	458
Country Units: Subjects			
Australia	42	62	64
Belgium	11	12	13
Denmark	5	8	7
France	32	45	45
Netherlands	5	8	6
Spain	4	6	5
United Kingdom	331	501	499
WHO Status Units: Subjects			
Zero	345	517	501
One	83	121	131
Two	0	0	1
Not recorded	2	4	6
Histology			

Units: Subjects			
Clear Cell	361	534	550
Papillary	33	58	37
Chromophobe	29	31	36
Collecting Duct	1	2	1
Other	6	17	15
Pathological T cat. of Primary Tumour			
Units: Subjects			
pT1a	3	2	2
pT1b	44	82	71
pT2	103	154	143
pT3a-4	280	404	423
Regional Lymph Node Status			
Units: Subjects			
pNx/pN0	412	619	606
pN1/pN2	18	23	33
Tumour Size			
Units: Subjects			
<10	286	436	430
>10	144	206	209
Nuclear Grade			
Units: Subjects			
One	19	38	32
Two	105	159	176
Three	222	323	314
Four	84	122	116
Not recorded	0	0	1
Histological Tumour Necrosis			
Units: Subjects			
No	192	284	298
Yes	238	358	341
Leibovich Score Group			
Units: Subjects			
Intermediate	224	342	344
High	206	300	295
Time from renal cell carcinoma diagnosis to randomisation			
Units: days			
arithmetic mean	84	82.2	83.2
full range (min-max)	11 to 201	-320 to 268	7 to 344

Reporting group values	Total		
Number of subjects	1711		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	1195		
From 65-84 years	515		
85 years and over	1		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	495		
Male	1216		
Country			
Units: Subjects			
Australia	168		
Belgium	36		
Denmark	20		
France	122		
Netherlands	19		
Spain	15		
United Kingdom	1331		
WHO Status			
Units: Subjects			
Zero	1363		
One	335		
Two	1		
Not recorded	12		
Histology			
Units: Subjects			
Clear Cell	1445		
Papillary	128		
Chromophobe	96		
Collecting Duct	4		
Other	38		
Pathological T cat. of Primary Tumour			
Units: Subjects			
pT1a	7		
pT1b	197		
pT2	400		
pT3a-4	1107		
Regional Lymph Node Status			
Units: Subjects			
pNx/pN0	1637		
pN1/pN2	74		
Tumour Size			
Units: Subjects			
<10	1152		
>10	559		
Nuclear Grade			
Units: Subjects			
One	89		

Two	440		
Three	859		
Four	322		
Not recorded	1		
Histological Tumour Necrosis			
Units: Subjects			
No	774		
Yes	937		
Leibovich Score Group			
Units: Subjects			
Intermediate	910		
High	801		
Time from renal cell carcinoma diagnosis to randomisation			
Units: days			
arithmetic mean			
full range (min-max)	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	1 Year Sorafenib + 2 Placebo
Reporting group description: -	
Reporting group title	3 Years Sorafenib
Reporting group description: -	

Primary: Disease free survival (DFS)

End point title	Disease free survival (DFS)
End point description:	
End point type	Primary
End point timeframe:	
DFS is the interval from randomisation to first evidence of local recurrence or distant metastases or death from RCC; if a trial participant hasn't experienced an event, their last time seen on trial is used.	

End point values	Placebo	1 Year Sorafenib + 2 Placebo	3 Years Sorafenib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	430	642	639	
Units: years				
median (inter-quartile range (Q1-Q3))	5.97 (1.82 to 7.64)	5.95 (2.26 to 7.66)	5.72 (2.11 to 7.23)	

Attachments (see zip file)	Kaplan-Meier; 1 Y Sor + 2 Y Plac vs Kaplan-Meier; 3 Y Sor vs Plac/SORCE_DFS_AvsC_KM.png
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Statistical analyses

Statistical analysis title	DFS 3 Years Sorafenib vs Placebo; HR
Comparison groups	3 Years Sorafenib v Placebo
Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.946
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.23

Statistical analysis title	DFS 3 Years Sorafenib vs Placebo; RMST
Comparison groups	3 Years Sorafenib v Placebo
Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.988
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.48

Statistical analysis title	DFS 1 Year Sor + 2 Plac vs Plac; HR
Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo
Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.509
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.14

Statistical analysis title	DFS 1 Year Sor + 2 Plac vs Plac; RMST
Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo

Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.422
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Mean difference (final values)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.65

Secondary: Metastasis free survival (MFS)

End point title	Metastasis free survival (MFS)
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End point description:

End point type	Secondary
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End point timeframe:

MFS is the interval from randomisation to first evidence of metastases or death from RCC; if a participant has not observed an event, their last time seen on trial is used.

End point values	Placebo	1 Year Sorafenib + 2 Placebo	3 Years Sorafenib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	430	642	639	
Units: years				
median (inter-quartile range (Q1-Q3))	5.98 (1.93 to 7.60)	5.97 (2.45 to 7.70)	5.80 (2.25 to 7.23)	

Attachments (see zip file)	Kaplan Meier Curves; MFS 3 Y Sor vs Kaplan Meier Curves; MFS 1 Y Sor + 2Y Plac vs
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Statistical analyses

Statistical analysis title	MFS 3 Year Sorafenib vs Placebo; HR
Comparison groups	3 Years Sorafenib v Placebo

Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.975
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.22

Statistical analysis title	MFS 3 Years Sorafenib vs Placebo; RMST
Comparison groups	3 Years Sorafenib v Placebo
Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.969
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.45

Statistical analysis title	MFS 1 Y Sor + 2 Y Placebo vs Placebo; HR
Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo
Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.313
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.1

Statistical analysis title	MFS 1 Y Sor + 2 Y Plac vs Placebo; RMST
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Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo
Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.273
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Log hazard ratio
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.74

Secondary: Renal Cell Carcinoma survival (RCCS)

End point title	Renal Cell Carcinoma survival (RCCS)
End point description:	
End point type	Secondary
End point timeframe:	
RCCS is the time from randomisation to death from RCC; if trial participants haven't experienced this event, their last time seen on trial is used.	

End point values	Placebo	1 Year Sorafenib + 2 Placebo	3 Years Sorafenib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	430	642	639	
Units: years				
median (inter-quartile range (Q1-Q3))	6.59 (4.90 to 8.03)	6.67 (4.94 to 8.02)	6.26 (4.68 to 7.98)	

Attachments (see zip file)	Kaplan Meier Curves; 3 Y Sor Vs Plac/SORCE_OS_AvsC_KM. Kaplan Meier Curves; 1 Y Sor + 2 Y Plac Vs
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Statistical analyses

Statistical analysis title	RCCS 3 Year Sorafenib vs Placebo; HR
Comparison groups	Placebo v 3 Years Sorafenib

Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.421
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.5

Statistical analysis title	RCCS 3 Years Sorafenib vs Placebo; RMST
Comparison groups	3 Years Sorafenib v Placebo
Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.423
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Mean difference (final values)
Point estimate	-0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.2

Statistical analysis title	RCCS 1 Y Sor + 2 Y Plac vs Plac; HR
Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo
Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.524
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.22

Statistical analysis title	RCCS 1 Y Sor + 2 Y Plac vs Plac; RSMT
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Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo
Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.439
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Mean difference (final values)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.46

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description:	
End point type	Secondary
End point timeframe:	OS is the time from randomisation to death from any cause, including RCC; if trial participants haven't experienced this event, their last time seen on trial is used.

End point values	Placebo	1 Year Sorafenib + 2 Placebo	3 Years Sorafenib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	430	642	639	
Units: years				
median (inter-quartile range (Q1-Q3))	6.69 (4.96 to 8.03)	6.68 (4.99 to 8.02)	6.29 (4.75 to 7.99)	

Attachments (see zip file)	Kaplan Meier Curves; OS 3 Y Sor vs Plac/SORCE_OS_AvsC_KM. Kaplan Meier Curves; OS 1 Y Sor + 2 Y Plac vs
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Statistical analyses

Statistical analysis title	OS 3 Year Sorafenib vs Placebo; HR
Comparison groups	3 Years Sorafenib v Placebo

Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.638
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.38

Statistical analysis title	OS 3 Year Sorafenib vs Placebo; RMST
Comparison groups	3 Years Sorafenib v Placebo
Number of subjects included in analysis	1069
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.711
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Mean difference (final values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.28

Statistical analysis title	OS 1 Y Sor + 2 Y Plac Vs Plac; HR
Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo
Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.541
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.2

Statistical analysis title	OS 1 Y Sor + 2 Y Plac Vs Plac;RMST
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Comparison groups	1 Year Sorafenib + 2 Placebo v Placebo
Number of subjects included in analysis	1072
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.453
Method	Restricted Mean Survival Tie Difference
Parameter estimate	Mean difference (final values)
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.49

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	BSor
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Reporting group description: -

Reporting group title	APlc
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Reporting group description: -

Reporting group title	CSor
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Reporting group description: -

Serious adverse events	BSor	APlc	CSor
Total subjects affected by serious adverse events			
subjects affected / exposed	135 / 642 (21.03%)	80 / 430 (18.60%)	147 / 639 (23.00%)
number of deaths (all causes)	132	96	143
number of deaths resulting from adverse events	3	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma	Additional description: B-cell lymphoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Basal cell carcinoma	Additional description: Basal cell carcinoma		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	3 / 639 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease	Additional description: Bowen's disease		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Breast cancer	Additional description: Breast cancer		

subjects affected / exposed	3 / 642 (0.47%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer in situ	Additional description: Breast cancer in situ		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondroma	Additional description: Chondroma		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia	Additional description: Chronic lymphocytic leukaemia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer	Additional description: Colon cancer		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Cutaneous T-cell lymphoma	Additional description: Cutaneous T-cell lymphoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Gastric cancer	Additional description: Gastric cancer		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Gastrointestinal stromal tumour	Additional description: Gastrointestinal stromal tumour		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Hormone receptor positive breast cancer	Additional description: Hormone receptor positive breast cancer		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma	Additional description: Invasive ductal breast carcinoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Intraductal proliferative breast lesion	Additional description: Intraductal proliferative breast lesion		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratoacanthoma	Additional description: Keratoacanthoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma	Additional description: Lung adenocarcinoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Lung neoplasm malignant	Additional description: Lung neoplasm malignant		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Malignant melanoma	Additional description: Malignant melanoma		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mantle cell lymphoma	Additional description: Mantle cell lymphoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Meningioma	Additional description: Meningioma		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Mesothelioma malignant	Additional description: Mesothelioma malignant		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Neoplasm malignant	Additional description: Neoplasm malignant		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Neuroendocrine tumour	Additional description: Neuroendocrine tumour		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Nodal marginal zone B-cell lymphoma	Additional description: Nodal marginal zone B-cell lymphoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Non-small cell lung cancer	Additional description: Non-small cell lung cancer		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Oesophageal carcinoma	Additional description: Oesophageal carcinoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Papillary cystadenoma lymphomatosum	Additional description: Papillary cystadenoma lymphomatosum		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary renal cell carcinoma	Additional description: Papillary renal cell carcinoma		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer	Additional description: Papillary thyroid cancer		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer	Additional description: Prostate cancer		
subjects affected / exposed	5 / 642 (0.78%)	6 / 430 (1.40%)	4 / 639 (0.63%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma	Additional description: Rectal adenocarcinoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Renal cancer	Additional description: Renal cancer		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy	Additional description: Second primary malignancy		
subjects affected / exposed	2 / 642 (0.31%)	3 / 430 (0.70%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Squamous cell carcinoma	Additional description: Squamous cell carcinoma		
subjects affected / exposed	10 / 642 (1.56%)	1 / 430 (0.23%)	12 / 639 (1.88%)
occurrences causally related to treatment / all	0 / 11	0 / 1	0 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial sarcoma	Additional description: Synovial sarcoma		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell cancer of the renal pelvis and ureter	Additional description: Transitional cell cancer of the renal pelvis and ureter		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Vascular disorders	Additional description: Aortic stenosis		
Aortic stenosis			
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial occlusive disease	Additional description: Arterial occlusive disease		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial spasm	Additional description: Arterial spasm		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	3 / 642 (0.47%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma	Additional description: Haematoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension	Additional description: Hypertension		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis	Additional description: Hypertensive crisis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Peripheral ischaemia	Additional description: Peripheral ischaemia		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis	Additional description: Thrombosis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cholecystectomy	Additional description: Cholecystectomy		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cyst drainage	Additional description: Cyst drainage		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Knee arthroplasty	Additional description: Knee arthroplasty		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin operation	Additional description: Skin operation		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Thyroidectomy	Additional description: Thyroidectomy		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adverse drug reaction	Additional description: Adverse drug reaction		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chest pain	Additional description: Chest pain		
subjects affected / exposed	9 / 642 (1.40%)	6 / 430 (1.40%)	8 / 639 (1.25%)
occurrences causally related to treatment / all	0 / 9	0 / 12	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills	Additional description: Chills		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Fatigue	Additional description: Fatigue		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome	Additional description: Multiple organ dysfunction syndrome		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	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	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain	Additional description: Pain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia	Additional description: Pyrexia		

subjects affected / exposed	3 / 642 (0.47%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suprapubic pain	Additional description: Suprapubic pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Immune system disorders			
Drug hypersensitivity	Additional description: Drug hypersensitivity		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis	Additional description: Sarcoidosis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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, thoracic and mediastinal disorders			
Asthma	Additional description: Asthma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemoptysis	Additional description: Haemoptysis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema	Additional description: Laryngeal oedema		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	1 / 642 (0.16%)	4 / 430 (0.93%)	5 / 639 (0.78%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary infarction	Additional description: Pulmonary infarction		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Pulmonary thrombosis	Additional description: Pulmonary thrombosis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation	Additional description: Disorientation		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Substance-induced psychotic disorder	Additional description: Substance-induced psychotic disorder		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Suicide attempt	Additional description: Suicide attempt		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest X-ray abnormal	Additional description: Chest X-ray abnormal		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Liver function test abnormal	Additional description: Liver function test abnormal		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic specific antigen increased	Additional description: Prostatic specific antigen increased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased	Additional description: Weight decreased		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Animal bite	Additional description: Animal bite		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture	Additional description: Ankle fracture		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Craniocerebral injury	Additional description: Craniocerebral injury		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Expired product administered	Additional description: Expired product administered		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Fall	Additional description: Fall		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Head injury	Additional description: Head injury		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Hip fracture	Additional description: Hip fracture		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Lower limb fracture	Additional description: Lower limb fracture		

subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose	Additional description: Overdose		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Subdural haematoma	Additional description: Subdural haematoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Traumatic fracture	Additional description: Traumatic fracture		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Cardiac disorders			
Acute coronary syndrome	Additional description: Acute coronary syndrome		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Acute myocardial infarction	Additional description: Acute myocardial infarction		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris	Additional description: Angina pectoris		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia	Additional description: Arrhythmia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriospasm coronary	Additional description: Arteriospasm coronary		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia	Additional description: Bradycardia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive	Additional description: Cardiac failure congestive		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	3 / 642 (0.47%)	4 / 430 (0.93%)	7 / 639 (1.10%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial ischaemia	Additional description: Myocardial ischaemia		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Palpitations	Additional description: Palpitations		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia	Additional description: Aphasia		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Cerebral haemorrhage	Additional description: Cerebral haemorrhage		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia	Additional description: Cerebral ischaemia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	3 / 639 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident	Additional description: Cerebrovascular accident		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	4 / 639 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness	Additional description: Dizziness		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dural arteriovenous fistula	Additional description: Dural arteriovenous fistula		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Headache	Additional description: Headache		
subjects affected / exposed	3 / 642 (0.47%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke	Additional description: Ischaemic stroke		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy	Additional description: Lethargy		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Loss of consciousness	Additional description: Loss of consciousness		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Multiple sclerosis	Additional description: Multiple sclerosis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage	Additional description: Subarachnoid haemorrhage		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Syncope	Additional description: Syncope		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia	Additional description: Transient global amnesia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack	Additional description: Transient ischaemic attack		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Eye disorders	Additional description: Amaurosis fugax		
Amaurosis fugax			
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Blindness	Additional description: Blindness		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Eye disorder	Additional description: Eye disorder		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Retinal vein occlusion	Additional description: Retinal vein occlusion		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal vein thrombosis	Additional description: Retinal vein thrombosis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative keratitis	Additional description: Ulcerative keratitis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders	Additional description: Abdominal discomfort		
Abdominal discomfort			
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Abdominal pain	Additional description: Abdominal pain		

subjects affected / exposed	5 / 642 (0.78%)	6 / 430 (1.40%)	8 / 639 (1.25%)
occurrences causally related to treatment / all	0 / 5	0 / 10	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower	Additional description: Abdominal pain lower		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	1 / 642 (0.16%)	3 / 430 (0.70%)	3 / 639 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall haematoma	Additional description: Abdominal wall haematoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Colitis	Additional description: Colitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Crohn's disease	Additional description: Crohn's disease		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Diaphragmatic hernia	Additional description: Diaphragmatic hernia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea	Additional description: Diarrhoea		

subjects affected / exposed	3 / 642 (0.47%)	1 / 430 (0.23%)	4 / 639 (0.63%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum	Additional description: Diverticulum		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Food poisoning	Additional description: Food poisoning		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Gastrointestinal haemorrhage	Additional description: Gastrointestinal haemorrhage		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis	Additional description: Haematemesis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Inguinal hernia	Additional description: Inguinal hernia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction	Additional description: Intestinal obstruction		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Intra-abdominal fluid collection	Additional description: Intra-abdominal fluid collection		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Large intestinal obstruction	Additional description: Large intestinal obstruction		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Oesophageal pain	Additional description: Oesophageal pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal spasm	Additional description: Oesophageal spasm		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Pancreatitis	Additional description: Pancreatitis		
subjects affected / exposed	4 / 642 (0.62%)	1 / 430 (0.23%)	3 / 639 (0.47%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage	Additional description: Rectal haemorrhage		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland disorder	Additional description: Salivary gland disorder		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Small intestinal obstruction	Additional description: Small intestinal obstruction		

subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	0 / 639 (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
Swollen tongue	Additional description: Swollen tongue		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Vomiting	Additional description: Vomiting		
subjects affected / exposed	0 / 642 (0.00%)	3 / 430 (0.70%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis	Additional description: Cholecystitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis	Additional description: Cholelithiasis		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure	Additional description: Hepatic failure		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Skin and subcutaneous tissue disorders			
Angioedema	Additional description: Angioedema		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis exfoliative generalised	Additional description: Dermatitis exfoliative generalised		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Erythema	Additional description: Erythema		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Erythema multiforme	Additional description: Erythema multiforme		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Hand and foot syndrome	Additional description: Hand and foot syndrome		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash	Additional description: Rash		
subjects affected / exposed	2 / 642 (0.31%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash erythematous	Additional description: Rash erythematous		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin toxicity	Additional description: Skin toxicity		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Skin ulcer	Additional description: Skin ulcer		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Bladder obstruction	Additional description: Bladder obstruction		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria	Additional description: Haematuria		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis	Additional description: Hydronephrosis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic nephropathy	Additional description: Ischaemic nephropathy		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Nephrolithiasis	Additional description: Nephrolithiasis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic	Additional description: Renal colic		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cyst	Additional description: Renal cyst		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure	Additional description: Renal failure		

subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (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
Renal impairment	Additional description: Renal impairment		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	0 / 639 (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
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Endocrine disorders			
Hypothalamo-pituitary disorder	Additional description: Hypothalamo-pituitary disorder		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain	Additional description: Back pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	3 / 639 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain	Additional description: Groin pain		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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

Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Myopathy	Additional description: Myopathy		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain	Additional description: Neck pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess	Additional description: Abscess		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess	Additional description: Anal abscess		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Appendicitis	Additional description: Appendicitis		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	3 / 642 (0.47%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis	Additional description: Cystitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Ear infection	Additional description: Ear infection		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas	Additional description: Erysipelas		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Furuncle	Additional description: Furuncle		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic infection	Additional description: Hepatic infection		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection	Additional description: Infection		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection	Additional description: Localised infection		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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 respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (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
Lymph gland infection	Additional description: Lymph gland infection		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (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
Pyelonephritis	Additional description: Pyelonephritis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Renal abscess	Additional description: Renal abscess		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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
Sepsis	Additional description: Sepsis		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (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
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	4 / 642 (0.62%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection	Additional description: Viral infection		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection	Additional description: Wound infection		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration	Additional description: Dehydration		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (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
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia	Additional description: Hypocalcaemia		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus	Additional description: Type 2 diabetes mellitus		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (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

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

Non-serious adverse events	BSor	APic	CSor
Total subjects affected by non-serious adverse events			
subjects affected / exposed	625 / 642 (97.35%)	414 / 430 (96.28%)	610 / 639 (95.46%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma	Additional description: Basal cell carcinoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	1	1
Breast cancer in situ	Additional description: Breast cancer in situ		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Elastofibroma	Additional description: Elastofibroma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Keratoacanthoma	Additional description: Keratoacanthoma		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Lipoma	Additional description: Lipoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Malignant melanoma	Additional description: Malignant melanoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Melanocytic naevus	Additional description: Melanocytic naevus		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	1	0	2

Meningioma	Additional description: Meningioma		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	0	2	0
Papillary cystadenoma lymphomatosum	Additional description: Papillary cystadenoma lymphomatosum		
	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed			
occurrences (all)	0	0	1
Pituitary tumour benign	Additional description: Pituitary tumour benign		
	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed			
occurrences (all)	0	0	2
Prostate cancer	Additional description: Prostate cancer		
	3 / 642 (0.47%)	2 / 430 (0.47%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	3	3	0
Second primary malignancy	Additional description: Second primary malignancy		
	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
subjects affected / exposed			
occurrences (all)	1	0	2
Skin papilloma	Additional description: Skin papilloma		
	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
subjects affected / exposed			
occurrences (all)	0	1	2
Squamous cell carcinoma	Additional description: Squamous cell carcinoma		
	2 / 642 (0.31%)	1 / 430 (0.23%)	5 / 639 (0.78%)
subjects affected / exposed			
occurrences (all)	2	1	9
Vascular disorders			
Aneurysm	Additional description: Aneurysm		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	1	0	0
Arterial spasm	Additional description: Arterial spasm		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	1	0	0
Arterial occlusive disease	Additional description: Arterial occlusive disease		
	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed			
occurrences (all)	0	0	1
Arteriosclerosis	Additional description: Arteriosclerosis		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	1	0	0
Deep vein thrombosis	Additional description: Deep vein thrombosis		

subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	2	1	1
Embolism	Additional description: Embolism		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Flushing	Additional description: Flushing		
subjects affected / exposed	15 / 642 (2.34%)	3 / 430 (0.70%)	11 / 639 (1.72%)
occurrences (all)	19	8	14
Haematoma	Additional description: Haematoma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	1	1
Hot flush	Additional description: Hot flush		
subjects affected / exposed	6 / 642 (0.93%)	5 / 430 (1.16%)	6 / 639 (0.94%)
occurrences (all)	12	8	9
Hypertension	Additional description: Hypertension		
subjects affected / exposed	377 / 642 (58.72%)	203 / 430 (47.21%)	394 / 639 (61.66%)
occurrences (all)	1545	999	1784
Hypotension	Additional description: Hypotension		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	2	0
Intermittent claudication	Additional description: Intermittent claudication		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Ischaemic limb pain	Additional description: Ischaemic limb pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Orthostatic hypotension	Additional description: Orthostatic hypotension		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Peripheral coldness	Additional description: Peripheral coldness		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	4
Phlebitis	Additional description: Phlebitis		
subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	2 / 639 (0.31%)
occurrences (all)	0	2	2
Thrombosis	Additional description: Thrombosis		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Varicose vein	Additional description: Varicose vein		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Appendicectomy	Additional description: Appendicectomy		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Artificial urinary sphincter implant	Additional description: Artificial urinary sphincter implant		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Bunion operation	Additional description: Bunion operation		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Cataract operation	Additional description: Cataract operation		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Cholecystectomy	Additional description: Cholecystectomy		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Coronary artery bypass	Additional description: Coronary artery bypass		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Cryotherapy	Additional description: Cryotherapy		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Elbow operation	Additional description: Elbow operation		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Gastric bypass	Additional description: Gastric bypass		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Genitourinary operation	Additional description: Genitourinary operation		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0

Hernia repair subjects affected / exposed occurrences (all)	Additional description: Hernia repair		
	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Lesion excision subjects affected / exposed occurrences (all)	Additional description: Lesion excision		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Lipoma excision subjects affected / exposed occurrences (all)	Additional description: Lipoma excision		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Nail operation subjects affected / exposed occurrences (all)	Additional description: Nail operation		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Steroid therapy subjects affected / exposed occurrences (all)	Additional description: Steroid therapy		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Therapy cessation subjects affected / exposed occurrences (all)	Additional description: Therapy cessation		
	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Tooth extraction subjects affected / exposed occurrences (all)	Additional description: Tooth extraction		
	3 / 642 (0.47%) 3	2 / 430 (0.47%) 2	2 / 639 (0.31%) 2
Tooth repair subjects affected / exposed occurrences (all)	Additional description: Tooth repair		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
General disorders and administration site conditions			
	Additional description: Asthenia		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	1 / 639 (0.16%) 4
	Additional description: Axillary pain		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Chest discomfort subjects affected / exposed occurrences (all)	Additional description: Chest discomfort		
	1 / 642 (0.16%) 1	2 / 430 (0.47%) 6	3 / 639 (0.47%) 3
Chest pain	Additional description: Chest pain		

subjects affected / exposed	8 / 642 (1.25%)	11 / 430 (2.56%)	14 / 639 (2.19%)
occurrences (all)	8	13	15
Chills	Additional description: Chills		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Cyst	Additional description: Cyst		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	2	2	0
Discomfort	Additional description: Discomfort		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Face oedema	Additional description: Face oedema		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Facial discomfort	Additional description: Facial discomfort		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Facial pain	Additional description: Facial pain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Fatigue	Additional description: Fatigue		
subjects affected / exposed	460 / 642 (71.65%)	256 / 430 (59.53%)	452 / 639 (70.74%)
occurrences (all)	1635	1144	1833
Feeling abnormal	Additional description: Feeling abnormal		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Feeling cold	Additional description: Feeling cold		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Feeling hot	Additional description: Feeling hot		
subjects affected / exposed	0 / 642 (0.00%)	3 / 430 (0.70%)	2 / 639 (0.31%)
occurrences (all)	0	3	3
Hernia	Additional description: Hernia		
subjects affected / exposed	0 / 642 (0.00%)	3 / 430 (0.70%)	0 / 639 (0.00%)
occurrences (all)	0	3	0
Hernia pain	Additional description: Hernia pain		

subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	3	2	3
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	1	1	4
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	3 / 642 (0.47%)	4 / 430 (0.93%)	2 / 639 (0.31%)
occurrences (all)	3	6	2
Malaise	Additional description: Malaise		
subjects affected / exposed	2 / 642 (0.31%)	3 / 430 (0.70%)	0 / 639 (0.00%)
occurrences (all)	2	3	0
Mucosal dryness	Additional description: Mucosal dryness		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Mucosal haemorrhage	Additional description: Mucosal haemorrhage		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	35 / 642 (5.45%)	12 / 430 (2.79%)	44 / 639 (6.89%)
occurrences (all)	54	15	67
Mucosal pain	Additional description: Mucosal pain		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Mucositis	Additional description: Mucositis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	14 / 642 (2.18%)	8 / 430 (1.86%)	4 / 639 (0.63%)
occurrences (all)	19	11	5
Oedema	Additional description: Oedema		
subjects affected / exposed	3 / 642 (0.47%)	3 / 430 (0.70%)	2 / 639 (0.31%)
occurrences (all)	3	3	2
Pain	Additional description: Pain		

subjects affected / exposed	39 / 642 (6.07%)	31 / 430 (7.21%)	30 / 639 (4.69%)
occurrences (all)	56	50	45
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	2 / 642 (0.31%)	3 / 430 (0.70%)	1 / 639 (0.16%)
occurrences (all)	2	3	1
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	6 / 642 (0.93%)	3 / 430 (0.70%)	2 / 639 (0.31%)
occurrences (all)	7	3	2
Suprapubic pain	Additional description: Suprapubic pain		
subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Swelling	Additional description: Swelling		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Swelling face	Additional description: Swelling face		
subjects affected / exposed	3 / 642 (0.47%)	0 / 430 (0.00%)	4 / 639 (0.63%)
occurrences (all)	3	0	5
Temperature intolerance	Additional description: Temperature intolerance		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	0	0	4
Tenderness	Additional description: Tenderness		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Ulcer	Additional description: Ulcer		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Xerosis	Additional description: Xerosis		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	1	2	2
Immune system disorders			
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	3 / 642 (0.47%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	4	1	1
Sarcoidosis	Additional description: Sarcoidosis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0

Seasonal allergy subjects affected / exposed occurrences (all)	Additional description: Seasonal allergy		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 2
Reproductive system and breast disorders			
	Additional description: Amenorrhoea		
Amenorrhoea subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Breast mass subjects affected / exposed occurrences (all)	Additional description: Breast mass		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Breast pain subjects affected / exposed occurrences (all)	Additional description: Breast pain		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Breast swelling subjects affected / exposed occurrences (all)	Additional description: Breast swelling		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Breast tenderness subjects affected / exposed occurrences (all)	Additional description: Breast tenderness		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Erectile dysfunction subjects affected / exposed occurrences (all)	Additional description: Erectile dysfunction		
	3 / 642 (0.47%) 4	4 / 430 (0.93%) 4	7 / 639 (1.10%) 14
Genital pain subjects affected / exposed occurrences (all)	Additional description: Genital pain		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Gynaecomastia subjects affected / exposed occurrences (all)	Additional description: Gynaecomastia		
	2 / 642 (0.31%) 3	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Hydrocele subjects affected / exposed occurrences (all)	Additional description: Hydrocele		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Menorrhagia subjects affected / exposed occurrences (all)	Additional description: Menorrhagia		
	6 / 642 (0.93%) 9	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Menstruation irregular	Additional description: Menstruation irregular		

subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Nipple enlargement	Additional description: Nipple enlargement		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	2	0	1
Nipple disorder	Additional description: Nipple disorder		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Nipple pain	Additional description: Nipple pain		
subjects affected / exposed	12 / 642 (1.87%)	0 / 430 (0.00%)	8 / 639 (1.25%)
occurrences (all)	12	0	10
Orchitis noninfective	Additional description: Orchitis noninfective		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Pelvic pain	Additional description: Pelvic pain		
subjects affected / exposed	1 / 642 (0.16%)	3 / 430 (0.70%)	0 / 639 (0.00%)
occurrences (all)	1	3	0
Perineal rash	Additional description: Perineal rash		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Perineal erythema	Additional description: Perineal erythema		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Prostatomegaly	Additional description: Prostatomegaly		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Scrotal pain	Additional description: Scrotal pain		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	3	0	0
Testicular mass	Additional description: Testicular mass		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed	2 / 642 (0.31%)	4 / 430 (0.93%)	1 / 639 (0.16%)
occurrences (all)	2	5	1
Testicular swelling	Additional description: Testicular swelling		

subjects affected / exposed	4 / 642 (0.62%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	5	2	0
Vaginal discharge	Additional description: Vaginal discharge		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	0	1	2
Vaginal haemorrhage	Additional description: Vaginal haemorrhage		
subjects affected / exposed	2 / 642 (0.31%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	3	4	0
Vulvovaginal inflammation	Additional description: Vulvovaginal inflammation		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal pain	Additional description: Vulvovaginal pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Vulvovaginal pruritus	Additional description: Vulvovaginal pruritus		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma	Additional description: Asthma		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	1	2	1
Bronchiectasis	Additional description: Bronchiectasis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Cough	Additional description: Cough		
subjects affected / exposed	14 / 642 (2.18%)	20 / 430 (4.65%)	16 / 639 (2.50%)
occurrences (all)	18	26	19
Dry throat	Additional description: Dry throat		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	29 / 642 (4.52%)	8 / 430 (1.86%)	41 / 639 (6.42%)
occurrences (all)	52	21	71
Dyspnoea	Additional description: Dyspnoea		

subjects affected / exposed	24 / 642 (3.74%)	23 / 430 (5.35%)	31 / 639 (4.85%)
occurrences (all)	50	37	42
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	8 / 642 (1.25%)	5 / 430 (1.16%)	16 / 639 (2.50%)
occurrences (all)	14	6	26
Lung disorder	Additional description: Lung disorder		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	3 / 642 (0.47%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	6	0	0
Nasal crusting	Additional description: Nasal crusting		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Nasal discomfort	Additional description: Nasal discomfort		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Nasal polyps	Additional description: Nasal polyps		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	5	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	12 / 642 (1.87%)	8 / 430 (1.86%)	11 / 639 (1.72%)
occurrences (all)	16	11	17
Pharyngeal swelling	Additional description: Pharyngeal swelling		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Productive cough	Additional description: Productive cough		
subjects affected / exposed	1 / 642 (0.16%)	3 / 430 (0.70%)	1 / 639 (0.16%)
occurrences (all)	1	3	2
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	2	0
Respiratory disorder	Additional description: Respiratory disorder		

subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	2	1	0
Rhinitis allergic	Additional description: Rhinitis allergic		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	4
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	3	1	2
Sinus congestion	Additional description: Sinus congestion		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Sinus disorder	Additional description: Sinus disorder		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	2
Sleep apnoea syndrome	Additional description: Sleep apnoea syndrome		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	3	1	0
Sputum discoloured	Additional description: Sputum discoloured		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Throat irritation	Additional description: Throat irritation		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	2	1
Psychiatric disorders			
Abnormal dreams	Additional description: Abnormal dreams		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Agitation	Additional description: Agitation		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	1	2	1
Anger	Additional description: Anger		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1

Anxiety subjects affected / exposed occurrences (all)	Additional description: Anxiety		
	7 / 642 (1.09%) 7	14 / 430 (3.26%) 20	8 / 639 (1.25%) 9
Confusional state subjects affected / exposed occurrences (all)	Additional description: Confusional state		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Depressed mood subjects affected / exposed occurrences (all)	Additional description: Depressed mood		
	2 / 642 (0.31%) 2	4 / 430 (0.93%) 4	9 / 639 (1.41%) 11
Depression subjects affected / exposed occurrences (all)	Additional description: Depression		
	8 / 642 (1.25%) 9	10 / 430 (2.33%) 15	17 / 639 (2.66%) 31
Emotional disorder subjects affected / exposed occurrences (all)	Additional description: Emotional disorder		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Frustration tolerance decreased subjects affected / exposed occurrences (all)	Additional description: Frustration tolerance decreased		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Insomnia subjects affected / exposed occurrences (all)	Additional description: Insomnia		
	8 / 642 (1.25%) 8	11 / 430 (2.56%) 21	7 / 639 (1.10%) 9
Irritability subjects affected / exposed occurrences (all)	Additional description: Irritability		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 4
Libido decreased subjects affected / exposed occurrences (all)	Additional description: Libido decreased		
	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	2 / 639 (0.31%) 4
Libido disorder subjects affected / exposed occurrences (all)	Additional description: Libido disorder		
	2 / 642 (0.31%) 2	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Loss of libido subjects affected / exposed occurrences (all)	Additional description: Loss of libido		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	2 / 639 (0.31%) 2
Mood altered subjects affected / exposed occurrences (all)	Additional description: Mood altered		
	7 / 642 (1.09%) 7	4 / 430 (0.93%) 4	9 / 639 (1.41%) 9

Mood swings subjects affected / exposed occurrences (all)	Additional description: Mood swings		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Nightmare subjects affected / exposed occurrences (all)	Additional description: Nightmare		
	1 / 642 (0.16%) 1	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Personality change subjects affected / exposed occurrences (all)	Additional description: Personality change		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Psychotic disorder subjects affected / exposed occurrences (all)	Additional description: Psychotic disorder		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Sleep disorder subjects affected / exposed occurrences (all)	Additional description: Sleep disorder		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Tearfulness subjects affected / exposed occurrences (all)	Additional description: Tearfulness		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Investigations			
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	Additional description: Activated partial thromboplastin time prolonged		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Adjusted calcium subjects affected / exposed occurrences (all)	Additional description: Adjusted calcium		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Alanine aminotransferase abnormal subjects affected / exposed occurrences (all)	Additional description: Alanine aminotransferase abnormal		
	2 / 642 (0.31%) 3	2 / 430 (0.47%) 3	1 / 639 (0.16%) 1
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	Additional description: Alanine aminotransferase increased		
	16 / 642 (2.49%) 20	5 / 430 (1.16%) 11	19 / 639 (2.97%) 27
Amylase abnormal subjects affected / exposed occurrences (all)	Additional description: Amylase abnormal		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Amylase increased	Additional description: Amylase increased		

subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	6 / 639 (0.94%)
occurrences (all)	3	2	7
Aspartate aminotransferase abnormal	Additional description: Aspartate aminotransferase abnormal		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	4 / 642 (0.62%)	2 / 430 (0.47%)	5 / 639 (0.78%)
occurrences (all)	4	2	5
Biopsy	Additional description: Biopsy		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Blood alkaline phosphatase abnormal	Additional description: Blood alkaline phosphatase abnormal		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	2
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	3 / 639 (0.47%)
occurrences (all)	2	0	4
Blood calcium decreased	Additional description: Blood calcium decreased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	0	0	2
Blood cholesterol increased	Additional description: Blood cholesterol increased		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	3	2	1
Blood creatine abnormal	Additional description: Blood creatine abnormal		
subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	0	2	2
Blood creatine increased	Additional description: Blood creatine increased		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Blood creatine phosphokinase	Additional description: Blood creatine phosphokinase		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased	Additional description: Blood creatine phosphokinase increased		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	5	0	1
Blood creatinine abnormal	Additional description: Blood creatinine abnormal		
subjects affected / exposed	2 / 642 (0.31%)	2 / 430 (0.47%)	3 / 639 (0.47%)
occurrences (all)	2	5	3
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	28 / 642 (4.36%)	28 / 430 (6.51%)	18 / 639 (2.82%)
occurrences (all)	44	49	27
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	0	1	3
Blood iron decreased	Additional description: Blood iron decreased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Blood lactate dehydrogenase abnormal	Additional description: Blood lactate dehydrogenase abnormal		
subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		
subjects affected / exposed	4 / 642 (0.62%)	4 / 430 (0.93%)	3 / 639 (0.47%)
occurrences (all)	5	5	5
Blood phosphorus abnormal	Additional description: Blood phosphorus abnormal		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Blood phosphorus decreased	Additional description: Blood phosphorus decreased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	4 / 639 (0.63%)
occurrences (all)	0	1	4
Blood potassium increased	Additional description: Blood potassium increased		
subjects affected / exposed	0 / 642 (0.00%)	3 / 430 (0.70%)	8 / 639 (1.25%)
occurrences (all)	0	4	10
Blood test abnormal	Additional description: Blood test abnormal		

subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Blood testosterone decreased	Additional description: Blood testosterone decreased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Blood triglycerides abnormal	Additional description: Blood triglycerides abnormal		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Blood urea abnormal	Additional description: Blood urea abnormal		
subjects affected / exposed	2 / 642 (0.31%)	3 / 430 (0.70%)	1 / 639 (0.16%)
occurrences (all)	2	8	2
Blood urea increased	Additional description: Blood urea increased		
subjects affected / exposed	2 / 642 (0.31%)	7 / 430 (1.63%)	3 / 639 (0.47%)
occurrences (all)	2	10	5
Blood uric acid increased	Additional description: Blood uric acid increased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Blood urine present	Additional description: Blood urine present		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	1	1
Colonoscopy	Additional description: Colonoscopy		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	1	0	2
Full blood count abnormal	Additional description: Full blood count abnormal		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase abnormal	Additional description: Gamma-glutamyltransferase abnormal		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	2 / 642 (0.31%)	3 / 430 (0.70%)	3 / 639 (0.47%)
occurrences (all)	2	3	3
Gastric pH increased	Additional description: Gastric pH increased		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	2	1
Globulins increased	Additional description: Globulins increased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Glomerular filtration rate decreased	Additional description: Glomerular filtration rate decreased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	3	0
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	4 / 642 (0.62%)	4 / 430 (0.93%)	6 / 639 (0.94%)
occurrences (all)	8	5	8
Hepatic enzyme increased	Additional description: Hepatic enzyme increased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Lipase increased	Additional description: Lipase increased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Liver function test increased	Additional description: Liver function test increased		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	2	0	1
Liver function test abnormal	Additional description: Liver function test abnormal		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	0	0	2
Monocyte count increased	Additional description: Monocyte count increased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Platelet analyses	Additional description: Platelet analyses		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	5	1	4
Prostatic specific antigen abnormal	Additional description: Prostatic specific antigen abnormal		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Prostatic specific antigen increased	Additional description: Prostatic specific antigen increased		
subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	5	4	0
Red blood cell count decreased	Additional description: Red blood cell count decreased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Rheumatoid factor	Additional description: Rheumatoid factor		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	0	0	3
Vitamin D decreased	Additional description: Vitamin D decreased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	11 / 642 (1.71%)	3 / 430 (0.70%)	7 / 639 (1.10%)
occurrences (all)	15	3	9
Weight increased	Additional description: Weight increased		
subjects affected / exposed	4 / 642 (0.62%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	6	1	2
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Ankle fracture	Additional description: Ankle fracture		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Arthropod bite	Additional description: Arthropod bite		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Burn oesophageal	Additional description: Burn oesophageal		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Contusion	Additional description: Contusion		
subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	5	2	0
Foot fracture	Additional description: Foot fracture		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Hand fracture	Additional description: Hand fracture		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	3 / 639 (0.47%)
occurrences (all)	0	0	4
Hernia pain	Additional description: Hernia pain		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Incisional hernia	Additional description: Incisional hernia		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Incision site complication	Additional description: Incision site complication		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	1	1	2
Inflammation of wound	Additional description: Inflammation of wound		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Joint injury	Additional description: Joint injury		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Ligament sprain	Additional description: Ligament sprain		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Meniscus injury	Additional description: Meniscus injury		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Muscle strain	Additional description: Muscle strain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Nail avulsion	Additional description: Nail avulsion		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Nail injury	Additional description: Nail injury		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Procedural pain	Additional description: Procedural pain		
subjects affected / exposed	2 / 642 (0.31%)	3 / 430 (0.70%)	0 / 639 (0.00%)
occurrences (all)	2	3	0
Rib fracture	Additional description: Rib fracture		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	1	1
Skin injury	Additional description: Skin injury		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	2 / 639 (0.31%)
occurrences (all)	1	2	2
Stoma complication	Additional description: Stoma complication		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Sunburn	Additional description: Sunburn		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	2	1	2
Thermal burn	Additional description: Thermal burn		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Tibia fracture	Additional description: Tibia fracture		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Trauma	Additional description: Trauma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Upper limb fracture	Additional description: Upper limb fracture		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Wound complication	Additional description: Wound complication		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Wrist fracture	Additional description: Wrist fracture		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders	Additional description: Angina pectoris		
Angina pectoris	3 / 642 (0.47%)	1 / 430 (0.23%)	1 / 639 (0.16%)
subjects affected / exposed	11	1	1
occurrences (all)	Additional description: Arrhythmia		
Arrhythmia	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
subjects affected / exposed	1	1	0
occurrences (all)	Additional description: Atrial fibrillation		
Atrial fibrillation	1 / 642 (0.16%)	2 / 430 (0.47%)	3 / 639 (0.47%)
subjects affected / exposed	2	4	3
occurrences (all)	Additional description: Atrioventricular block		
Atrioventricular block	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed	0	0	1
occurrences (all)	Additional description: Atrioventricular block second degree		
Atrioventricular block second degree	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed	0	0	1
occurrences (all)	Additional description: Bradycardia		
Bradycardia	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed	0	0	1
occurrences (all)	Additional description: Cardiac disorder		
Cardiac disorder	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed	0	0	1
occurrences (all)	Additional description: Cardiac valve disease		
Cardiac valve disease	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed	1	0	0
occurrences (all)	Additional description: Extrasystoles		
Extrasystoles	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed	2	0	0
occurrences (all)	Additional description: Myocardial infarction		
Myocardial infarction	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
subjects affected / exposed	1	0	2
occurrences (all)	Additional description: Myocardial ischaemia		
Myocardial ischaemia	0 / 642 (0.00%)	0 / 430 (0.00%)	3 / 639 (0.47%)
subjects affected / exposed	0	0	3
occurrences (all)			

Palpitations subjects affected / exposed occurrences (all)	Additional description: Palpitations		
	3 / 642 (0.47%)	5 / 430 (1.16%)	0 / 639 (0.00%)
	3	5	0
Nervous system disorders			
	Additional description: Ageusia		
Ageusia subjects affected / exposed occurrences (all)	0 / 642 (0.00%)	3 / 430 (0.70%)	1 / 639 (0.16%)
	0	5	1
Amnesia	Additional description: Amnesia		
	1 / 642 (0.16%)	3 / 430 (0.70%)	1 / 639 (0.16%)
subjects affected / exposed occurrences (all)	1	4	1
Anosmia	Additional description: Anosmia		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
subjects affected / exposed occurrences (all)	0	1	0
Aphasia	Additional description: Aphasia		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed occurrences (all)	1	0	0
Balance disorder	Additional description: Balance disorder		
	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
subjects affected / exposed occurrences (all)	0	1	1
Burning sensation	Additional description: Burning sensation		
	1 / 642 (0.16%)	4 / 430 (0.93%)	1 / 639 (0.16%)
subjects affected / exposed occurrences (all)	1	6	1
Carpal tunnel syndrome	Additional description: Carpal tunnel syndrome		
	0 / 642 (0.00%)	3 / 430 (0.70%)	1 / 639 (0.16%)
subjects affected / exposed occurrences (all)	0	5	1
Cluster headache	Additional description: Cluster headache		
	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed occurrences (all)	0	0	1
Cognitive and attention disorders and disturbances NEC	Additional description: Cognitive and attention disorders and disturbances NEC		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
subjects affected / exposed occurrences (all)	0	4	0
Diabetic neuropathy	Additional description: Diabetic neuropathy		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed occurrences (all)	1	0	0
Disturbance in attention	Additional description: Disturbance in attention		

subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	0	7	0
Dizziness	Additional description: Dizziness		
subjects affected / exposed	15 / 642 (2.34%)	21 / 430 (4.88%)	8 / 639 (1.25%)
occurrences (all)	20	25	11
Dizziness postural	Additional description: Dizziness postural		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Dysaesthesia	Additional description: Dysaesthesia		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	1	0	3
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	4 / 642 (0.62%)	2 / 430 (0.47%)	7 / 639 (1.10%)
occurrences (all)	4	6	8
Facial paralysis	Additional description: Facial paralysis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Head discomfort	Additional description: Head discomfort		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Headache	Additional description: Headache		
subjects affected / exposed	50 / 642 (7.79%)	35 / 430 (8.14%)	55 / 639 (8.61%)
occurrences (all)	73	58	68
Hydrocephalus	Additional description: Hydrocephalus		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Hyperaesthesia	Additional description: Hyperaesthesia		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	4	0
Lethargy	Additional description: Lethargy		
subjects affected / exposed	4 / 642 (0.62%)	0 / 430 (0.00%)	4 / 639 (0.63%)
occurrences (all)	4	0	7
Loss of consciousness	Additional description: Loss of consciousness		

subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	1	3	1
Memory impairment	Additional description: Memory impairment		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	3
Migraine	Additional description: Migraine		
subjects affected / exposed	5 / 642 (0.78%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	5	2	2
Nervous system disorder	Additional description: Nervous system disorder		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	1	0	2
Neuralgia	Additional description: Neuralgia		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	0	2	5
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	7 / 642 (1.09%)	4 / 430 (0.93%)	10 / 639 (1.56%)
occurrences (all)	8	4	10
Neurotoxicity	Additional description: Neurotoxicity		
subjects affected / exposed	3 / 642 (0.47%)	1 / 430 (0.23%)	3 / 639 (0.47%)
occurrences (all)	4	1	3
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	18 / 642 (2.80%)	14 / 430 (3.26%)	18 / 639 (2.82%)
occurrences (all)	23	29	29
Parkinson's disease	Additional description: Parkinson's disease		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Peripheral motor neuropathy	Additional description: Peripheral motor neuropathy		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	1	2	0
Poor quality sleep	Additional description: Poor quality sleep		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Psychomotor hyperactivity	Additional description: Psychomotor hyperactivity		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	0
Resting tremor	Additional description: Resting tremor		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Restless legs syndrome	Additional description: Restless legs syndrome		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Sciatica	Additional description: Sciatica		
subjects affected / exposed	4 / 642 (0.62%)	3 / 430 (0.70%)	4 / 639 (0.63%)
occurrences (all)	4	11	7
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Sensory neuropathy	Additional description: Sensory neuropathy		
subjects affected / exposed	4 / 642 (0.62%)	2 / 430 (0.47%)	8 / 639 (1.25%)
occurrences (all)	9	10	14
Sinus headache	Additional description: Sinus headache		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Somnolence	Additional description: Somnolence		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	1	1	1
Syncope	Additional description: Syncope		
subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	4 / 639 (0.63%)
occurrences (all)	3	2	4
Taste disorder	Additional description: Taste disorder		
subjects affected / exposed	1 / 642 (0.16%)	5 / 430 (1.16%)	5 / 639 (0.78%)
occurrences (all)	1	9	7
Transient global amnesia	Additional description: Transient global amnesia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Transient ischaemic attack	Additional description: Transient ischaemic attack		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	2	0	2
Tremor	Additional description: Tremor		

subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	5	0	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	7 / 642 (1.09%)	8 / 430 (1.86%)	5 / 639 (0.78%)
occurrences (all)	9	8	7
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	2 / 642 (0.31%)	3 / 430 (0.70%)	0 / 639 (0.00%)
occurrences (all)	4	5	0
Platelet disorder	Additional description: Platelet disorder		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	3 / 639 (0.47%)
occurrences (all)	1	1	3
Thrombocytosis	Additional description: Thrombocytosis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Deafness	Additional description: Deafness		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	3	0	5
Ear congestion	Additional description: Ear congestion		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Ear pain	Additional description: Ear pain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	3 / 639 (0.47%)
occurrences (all)	0	0	3
Eustachian tube dysfunction	Additional description: Eustachian tube dysfunction		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	5	0	2
Hypoacusis	Additional description: Hypoacusis		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Tinnitus	Additional description: Tinnitus		
subjects affected / exposed	1 / 642 (0.16%)	6 / 430 (1.40%)	8 / 639 (1.25%)
occurrences (all)	2	13	12
Vertigo	Additional description: Vertigo		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	1	1
Eye disorders			
Amaurosis fugax	Additional description: Amaurosis fugax		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Astigmatism	Additional description: Astigmatism		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Blindness	Additional description: Blindness		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Chalazion	Additional description: Chalazion		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Conjunctival haemorrhage	Additional description: Conjunctival haemorrhage		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Dry eye	Additional description: Dry eye		
subjects affected / exposed	1 / 642 (0.16%)	3 / 430 (0.70%)	3 / 639 (0.47%)
occurrences (all)	4	3	4
Eye haemorrhage	Additional description: Eye haemorrhage		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Eye irritation	Additional description: Eye irritation		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	1	1	2
Eye pain	Additional description: Eye pain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1

Eye pruritus subjects affected / exposed occurrences (all)	Additional description: Eye pruritus		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Eye swelling subjects affected / exposed occurrences (all)	Additional description: Eye swelling		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	2 / 639 (0.31%) 2
Eyelid cyst subjects affected / exposed occurrences (all)	Additional description: Eyelid cyst		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Eyelid irritation subjects affected / exposed occurrences (all)	Additional description: Eyelid irritation		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Eyelid oedema subjects affected / exposed occurrences (all)	Additional description: Eyelid oedema		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Foreign body sensation in eyes subjects affected / exposed occurrences (all)	Additional description: Foreign body sensation in eyes		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Glaucoma subjects affected / exposed occurrences (all)	Additional description: Glaucoma		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Iritis subjects affected / exposed occurrences (all)	Additional description: Iritis		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	2 / 639 (0.31%) 2
Keratitis subjects affected / exposed occurrences (all)	Additional description: Keratitis		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Lacrimation increased subjects affected / exposed occurrences (all)	Additional description: Lacrimation increased		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Ocular hyperaemia subjects affected / exposed occurrences (all)	Additional description: Ocular hyperaemia		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Periorbital swelling subjects affected / exposed occurrences (all)	Additional description: Periorbital swelling		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0

Periorbital oedema subjects affected / exposed occurrences (all)	Additional description: Periorbital oedema		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
	Additional description: Retinal detachment		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
	Additional description: Retinal haemorrhage		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Retinal vein occlusion subjects affected / exposed occurrences (all)	Additional description: Retinal vein occlusion		
	3 / 642 (0.47%) 13	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	Additional description: Vision blurred		
	2 / 642 (0.31%) 2	2 / 430 (0.47%) 6	3 / 639 (0.47%) 3
Visual impairment subjects affected / exposed occurrences (all)	Additional description: Visual impairment		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 2
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	Additional description: Abdominal discomfort		
	6 / 642 (0.93%) 6	4 / 430 (0.93%) 4	4 / 639 (0.63%) 4
	Additional description: Abdominal distension		
	9 / 642 (1.40%) 10	8 / 430 (1.86%) 14	6 / 639 (0.94%) 6
	Additional description: Abdominal hernia		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 6	0 / 639 (0.00%) 0
	Additional description: Abdominal pain		
Abdominal pain subjects affected / exposed occurrences (all)	39 / 642 (6.07%) 49	32 / 430 (7.44%) 50	53 / 639 (8.29%) 85
	Additional description: Abdominal pain lower		
Abdominal pain lower subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	5 / 430 (1.16%) 8	4 / 639 (0.63%) 5
	Additional description: Abdominal pain upper		
Abdominal pain upper			

subjects affected / exposed	20 / 642 (3.12%)	10 / 430 (2.33%)	22 / 639 (3.44%)
occurrences (all)	27	12	31
Abdominal tenderness	Additional description: Abdominal tenderness		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Abnormal faeces	Additional description: Abnormal faeces		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Anal fissure	Additional description: Anal fissure		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Anal haemorrhage	Additional description: Anal haemorrhage		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	1	1
Anal inflammation	Additional description: Anal inflammation		
subjects affected / exposed	3 / 642 (0.47%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	3	0	0
Anal pruritus	Additional description: Anal pruritus		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Aphthous ulcer	Additional description: Aphthous ulcer		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Change of bowel habit	Additional description: Change of bowel habit		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	3	1	0
Colitis	Additional description: Colitis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Constipation	Additional description: Constipation		
subjects affected / exposed	64 / 642 (9.97%)	28 / 430 (6.51%)	57 / 639 (8.92%)
occurrences (all)	95	53	86
Defaecation urgency	Additional description: Defaecation urgency		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Dental caries	Additional description: Dental caries		

subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	379 / 642 (59.03%)	134 / 430 (31.16%)	391 / 639 (61.19%)
occurrences (all)	1054	307	1644
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	5 / 642 (0.78%)	8 / 430 (1.86%)	2 / 639 (0.31%)
occurrences (all)	6	9	2
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	23 / 642 (3.58%)	19 / 430 (4.42%)	19 / 639 (2.97%)
occurrences (all)	31	43	35
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	4 / 639 (0.63%)
occurrences (all)	1	1	5
Epigastric discomfort	Additional description: Epigastric discomfort		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	0	1	2
Faecaloma	Additional description: Faecaloma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured	Additional description: Faeces discoloured		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Flatulence	Additional description: Flatulence		
subjects affected / exposed	6 / 642 (0.93%)	2 / 430 (0.47%)	3 / 639 (0.47%)
occurrences (all)	7	3	6
Food poisoning	Additional description: Food poisoning		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements	Additional description: Frequent bowel movements		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	2	1	0
Gastric ulcer	Additional description: Gastric ulcer		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Gastritis	Additional description: Gastritis		

subjects affected / exposed	0 / 642 (0.00%)	3 / 430 (0.70%)	1 / 639 (0.16%)
occurrences (all)	0	3	1
Gastrointestinal disorder	Additional description: Gastrointestinal disorder		
subjects affected / exposed	6 / 642 (0.93%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	6	0	1
Gastrointestinal haemorrhage	Additional description: Gastrointestinal haemorrhage		
subjects affected / exposed	6 / 642 (0.93%)	1 / 430 (0.23%)	7 / 639 (1.10%)
occurrences (all)	7	1	7
Gastrointestinal mucocoele	Additional description: Gastrointestinal mucocoele		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal obstruction	Additional description: Gastrointestinal obstruction		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Gastrointestinal pain	Additional description: Gastrointestinal pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	8 / 642 (1.25%)	3 / 430 (0.70%)	8 / 639 (1.25%)
occurrences (all)	9	5	11
Gingival bleeding	Additional description: Gingival bleeding		
subjects affected / exposed	7 / 642 (1.09%)	2 / 430 (0.47%)	6 / 639 (0.94%)
occurrences (all)	7	3	6
Gingival pain	Additional description: Gingival pain		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	2	0	1
Gingival ulceration	Additional description: Gingival ulceration		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Glossitis	Additional description: Glossitis		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	2	0	1
Glossodynia	Additional description: Glossodynia		
subjects affected / exposed	11 / 642 (1.71%)	0 / 430 (0.00%)	10 / 639 (1.56%)
occurrences (all)	23	0	16
Haematemesis	Additional description: Haematemesis		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Haematochezia	Additional description: Haematochezia		
subjects affected / exposed	0 / 642 (0.00%)	5 / 430 (1.16%)	1 / 639 (0.16%)
occurrences (all)	0	6	1
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	5 / 642 (0.78%)	1 / 430 (0.23%)	6 / 639 (0.94%)
occurrences (all)	6	1	8
Hhaemorrhoids	Additional description: Hhaemorrhoids		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Hypoaesthesia oral	Additional description: Hypoaesthesia oral		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Inguinal hernia	Additional description: Inguinal hernia		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Intra-abdominal fluid collection	Additional description: Intra-abdominal fluid collection		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Lip swelling	Additional description: Lip swelling		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Lower gastrointestinal haemorrhage	Additional description: Lower gastrointestinal haemorrhage		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Mouth haemorrhage	Additional description: Mouth haemorrhage		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	0	1	2
Mouth ulceration	Additional description: Mouth ulceration		
subjects affected / exposed	12 / 642 (1.87%)	6 / 430 (1.40%)	12 / 639 (1.88%)
occurrences (all)	13	9	12
Mucous stools	Additional description: Mucous stools		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Nausea	Additional description: Nausea		

subjects affected / exposed	211 / 642 (32.87%)	111 / 430 (25.81%)	186 / 639 (29.11%)
occurrences (all)	385	264	390
Oesophagitis	Additional description: Oesophagitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Oral discomfort	Additional description: Oral discomfort		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Oral pain	Additional description: Oral pain		
subjects affected / exposed	21 / 642 (3.27%)	9 / 430 (2.09%)	30 / 639 (4.69%)
occurrences (all)	27	13	40
Pancreatic insufficiency	Additional description: Pancreatic insufficiency		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Pancreatitis	Additional description: Pancreatitis		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	4	0	1
Pancreatitis acute	Additional description: Pancreatitis acute		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Paraesthesia oral	Additional description: Paraesthesia oral		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Proctalgia	Additional description: Proctalgia		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	4	0	2
Proctitis	Additional description: Proctitis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Rectal haemorrhage	Additional description: Rectal haemorrhage		
subjects affected / exposed	3 / 642 (0.47%)	4 / 430 (0.93%)	6 / 639 (0.94%)
occurrences (all)	3	5	8
Salivary gland disorder	Additional description: Salivary gland disorder		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Salivary gland enlargement	Additional description: Salivary gland enlargement		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	60 / 642 (9.35%)	17 / 430 (3.95%)	63 / 639 (9.86%)
occurrences (all)	92	32	105
Swollen tongue	Additional description: Swollen tongue		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Tongue discolouration	Additional description: Tongue discolouration		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Tongue ulceration	Additional description: Tongue ulceration		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	2	1	1
Tongue dry	Additional description: Tongue dry		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Tooth disorder	Additional description: Tooth disorder		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Toothache	Additional description: Toothache		
subjects affected / exposed	2 / 642 (0.31%)	2 / 430 (0.47%)	4 / 639 (0.63%)
occurrences (all)	4	2	9
Umbilical hernia	Additional description: Umbilical hernia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Vomiting	Additional description: Vomiting		
subjects affected / exposed	26 / 642 (4.05%)	10 / 430 (2.33%)	26 / 639 (4.07%)
occurrences (all)	32	12	39
Hepatobiliary disorders			
Biliary colic	Additional description: Biliary colic		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Cholecystitis	Additional description: Cholecystitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1

Cholelithiasis subjects affected / exposed occurrences (all)	Additional description: Cholelithiasis		
	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	2 / 639 (0.31%) 3
Hepatitis cholestatic subjects affected / exposed occurrences (all)	Additional description: Hepatitis cholestatic		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Hepatocellular injury subjects affected / exposed occurrences (all)	Additional description: Hepatocellular injury		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	Additional description: Hyperbilirubinaemia		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed occurrences (all)	Additional description: Acne		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Alopecia subjects affected / exposed occurrences (all)	Additional description: Alopecia		
	338 / 642 (52.65%) 703	53 / 430 (12.33%) 112	304 / 639 (47.57%) 787
Angioedema subjects affected / exposed occurrences (all)	Additional description: Angioedema		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Blister subjects affected / exposed occurrences (all)	Additional description: Blister		
	4 / 642 (0.62%) 4	1 / 430 (0.23%) 1	2 / 639 (0.31%) 2
Blood blister subjects affected / exposed occurrences (all)	Additional description: Blood blister		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 2
Dandruff subjects affected / exposed occurrences (all)	Additional description: Dandruff		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Dermatitis subjects affected / exposed occurrences (all)	Additional description: Dermatitis		
	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Dermatitis contact	Additional description: Dermatitis contact		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Dermatitis exfoliative generalised	Additional description: Dermatitis exfoliative generalised		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	2	0	1
Dry skin	Additional description: Dry skin		
subjects affected / exposed	46 / 642 (7.17%)	25 / 430 (5.81%)	39 / 639 (6.10%)
occurrences (all)	71	55	70
Dyshidrotic eczema	Additional description: Dyshidrotic eczema		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Eczema	Additional description: Eczema		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	2	1	0
Eczema asteatotic	Additional description: Eczema asteatotic		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Erythema	Additional description: Erythema		
subjects affected / exposed	18 / 642 (2.80%)	5 / 430 (1.16%)	12 / 639 (1.88%)
occurrences (all)	23	5	17
Furuncle	Additional description: Furuncle		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Haemorrhage subcutaneous	Additional description: Haemorrhage subcutaneous		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Hair colour changes	Additional description: Hair colour changes		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	3 / 639 (0.47%)
occurrences (all)	2	0	4
Hair growth abnormal	Additional description: Hair growth abnormal		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	1	0	2
Hair texture abnormal	Additional description: Hair texture abnormal		
subjects affected / exposed	5 / 642 (0.78%)	1 / 430 (0.23%)	3 / 639 (0.47%)
occurrences (all)	5	1	6
Hand and foot syndrome	Additional description: Hand and foot syndrome		

subjects affected / exposed	491 / 642 (76.48%)	135 / 430 (31.40%)	473 / 639 (74.02%)
occurrences (all)	1566	338	1910
Hidradenitis	Additional description: Hidradenitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	4 / 642 (0.62%)	2 / 430 (0.47%)	6 / 639 (0.94%)
occurrences (all)	4	3	10
Hyperkeratosis	Additional description: Hyperkeratosis		
subjects affected / exposed	7 / 642 (1.09%)	1 / 430 (0.23%)	10 / 639 (1.56%)
occurrences (all)	9	3	17
Miliaria	Additional description: Miliaria		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Mucocutaneous rash	Additional description: Mucocutaneous rash		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Nail disorder	Additional description: Nail disorder		
subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	3 / 639 (0.47%)
occurrences (all)	3	5	4
Nail pitting	Additional description: Nail pitting		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Nail psoriasis	Additional description: Nail psoriasis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Nail ridging	Additional description: Nail ridging		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Neurodermatitis	Additional description: Neurodermatitis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Night sweats	Additional description: Night sweats		
subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	3	2	1
Onychalgia	Additional description: Onychalgia		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Onychoclasia	Additional description: Onychoclasia		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	12	0
Pain of skin	Additional description: Pain of skin		
subjects affected / exposed	23 / 642 (3.58%)	6 / 430 (1.40%)	27 / 639 (4.23%)
occurrences (all)	33	25	34
Palmar-plantar erythrodysesthesia syndrome	Additional description: Palmar-plantar erythrodysesthesia syndrome		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	4	0
Photosensitivity reaction	Additional description: Photosensitivity reaction		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	2	0	5
Pigmentation disorder	Additional description: Pigmentation disorder		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Plantar erythema	Additional description: Plantar erythema		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Pruritis	Additional description: Pruritis		
subjects affected / exposed	25 / 642 (3.89%)	9 / 430 (2.09%)	28 / 639 (4.38%)
occurrences (all)	33	9	43
Pruritus	Additional description: Pruritus		
subjects affected / exposed	48 / 642 (7.48%)	25 / 430 (5.81%)	64 / 639 (10.02%)
occurrences (all)	68	34	93
Psoriasis	Additional description: Psoriasis		
subjects affected / exposed	8 / 642 (1.25%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	12	1	11
Rash	Additional description: Rash		
subjects affected / exposed	439 / 642 (68.38%)	130 / 430 (30.23%)	437 / 639 (68.39%)
occurrences (all)	1110	305	1174
Rash papular	Additional description: Rash papular		
subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	6 / 639 (0.94%)
occurrences (all)	3	4	9

Scar pain	Additional description: Scar pain		
	12 / 642 (1.87%)	21 / 430 (4.88%)	13 / 639 (2.03%)
	13	34	16
Skin atrophy	Additional description: Skin atrophy		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
	1	0	0
Skin depigmentation	Additional description: Skin depigmentation		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
	0	1	0
Skin discolouration	Additional description: Skin discolouration		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
	1	0	0
Skin disorder	Additional description: Skin disorder		
	2 / 642 (0.31%)	3 / 430 (0.70%)	5 / 639 (0.78%)
	2	3	5
Skin exfoliation	Additional description: Skin exfoliation		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
	2	0	0
Skin fissures	Additional description: Skin fissures		
	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
	0	0	1
Skin hypertrophy	Additional description: Skin hypertrophy		
	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
	0	1	1
Skin irritation	Additional description: Skin irritation		
	4 / 642 (0.62%)	0 / 430 (0.00%)	1 / 639 (0.16%)
	7	0	1
Skin lesion	Additional description: Skin lesion		
	4 / 642 (0.62%)	1 / 430 (0.23%)	4 / 639 (0.63%)
	6	1	5
Skin mass	Additional description: Skin mass		
	1 / 642 (0.16%)	1 / 430 (0.23%)	2 / 639 (0.31%)
	1	1	2
Skin papilloma	Additional description: Skin papilloma		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
	1	0	0

Skin reaction subjects affected / exposed occurrences (all)	Additional description: Skin reaction		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Skin swelling subjects affected / exposed occurrences (all)	Additional description: Skin swelling		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Skin tightness subjects affected / exposed occurrences (all)	Additional description: Skin tightness		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	2 / 639 (0.31%) 2
Skin toxicity subjects affected / exposed occurrences (all)	Additional description: Skin toxicity		
	1 / 642 (0.16%) 2	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Skin ulcer subjects affected / exposed occurrences (all)	Additional description: Skin ulcer		
	1 / 642 (0.16%) 2	0 / 430 (0.00%) 0	1 / 639 (0.16%) 2
Splinter haemorrhages subjects affected / exposed occurrences (all)	Additional description: Splinter haemorrhages		
	2 / 642 (0.31%) 2	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Toxic skin eruption subjects affected / exposed occurrences (all)	Additional description: Toxic skin eruption		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Urticaria subjects affected / exposed occurrences (all)	Additional description: Urticaria		
	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Renal and urinary disorders			
Bladder pain subjects affected / exposed occurrences (all)	Additional description: Bladder pain		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Chromaturia subjects affected / exposed occurrences (all)	Additional description: Chromaturia		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Dysuria subjects affected / exposed occurrences (all)	Additional description: Dysuria		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 4	2 / 639 (0.31%) 3
Haematuria	Additional description: Haematuria		

subjects affected / exposed	3 / 642 (0.47%)	3 / 430 (0.70%)	4 / 639 (0.63%)
occurrences (all)	3	7	5
Hypertonic bladder	Additional description: Hypertonic bladder		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Lower urinary tract symptoms	Additional description: Lower urinary tract symptoms		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Micturition urgency	Additional description: Micturition urgency		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	5	1	2
Nephrolithiasis	Additional description: Nephrolithiasis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Nocturia	Additional description: Nocturia		
subjects affected / exposed	5 / 642 (0.78%)	6 / 430 (1.40%)	3 / 639 (0.47%)
occurrences (all)	7	18	3
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	4 / 642 (0.62%)	5 / 430 (1.16%)	3 / 639 (0.47%)
occurrences (all)	5	9	3
Polyuria	Additional description: Polyuria		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Proteinuria	Additional description: Proteinuria		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	2 / 639 (0.31%)
occurrences (all)	1	2	2
Renal colic	Additional description: Renal colic		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Renal failure	Additional description: Renal failure		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	3	0
Renal pain	Additional description: Renal pain		
subjects affected / exposed	1 / 642 (0.16%)	4 / 430 (0.93%)	2 / 639 (0.31%)
occurrences (all)	1	5	2
Renal vein occlusion	Additional description: Renal vein occlusion		

subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Urethral haemorrhage	Additional description: Urethral haemorrhage		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Urethral stenosis	Additional description: Urethral stenosis		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Urinary incontinence	Additional description: Urinary incontinence		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Urinary tract disorder	Additional description: Urinary tract disorder		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Urine abnormality	Additional description: Urine abnormality		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperparathyroidism	Additional description: Hyperparathyroidism		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	3	0
Hyperthyroidism	Additional description: Hyperthyroidism		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	2	0
Hypogonadism	Additional description: Hypogonadism		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0

Hypothyroidism subjects affected / exposed occurrences (all)	Additional description: Hypothyroidism		
	2 / 642 (0.31%) 2	0 / 430 (0.00%) 0	2 / 639 (0.31%) 4
Parathyroid disorder subjects affected / exposed occurrences (all)	Additional description: Parathyroid disorder		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Thyroid mass subjects affected / exposed occurrences (all)	Additional description: Thyroid mass		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Thyroid disorder subjects affected / exposed occurrences (all)	Additional description: Thyroid disorder		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Thyroiditis subjects affected / exposed occurrences (all)	Additional description: Thyroiditis		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Musculoskeletal and connective tissue disorders			
	Additional description: Abdominal pain upper		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	Additional description: Arthralgia		
	48 / 642 (7.48%) 69	57 / 430 (13.26%) 100	48 / 639 (7.51%) 65
Arthritis subjects affected / exposed occurrences (all)	Additional description: Arthritis		
	5 / 642 (0.78%) 5	8 / 430 (1.86%) 13	5 / 639 (0.78%) 5
Arthropathy subjects affected / exposed occurrences (all)	Additional description: Arthropathy		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Axillary pain subjects affected / exposed occurrences (all)	Additional description: Axillary pain		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	Additional description: Back pain		
	44 / 642 (6.85%) 69	72 / 430 (16.74%) 125	44 / 639 (6.89%) 74
Bone pain	Additional description: Bone pain		

subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Bursitis	Additional description: Bursitis		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	1	1	0
Fibromyalgia	Additional description: Fibromyalgia		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Fistula	Additional description: Fistula		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Flank pain	Additional description: Flank pain		
subjects affected / exposed	6 / 642 (0.93%)	12 / 430 (2.79%)	8 / 639 (1.25%)
occurrences (all)	8	17	12
Groin pain	Additional description: Groin pain		
subjects affected / exposed	6 / 642 (0.93%)	7 / 430 (1.63%)	3 / 639 (0.47%)
occurrences (all)	7	11	3
Intervertebral disc protrusion	Additional description: Intervertebral disc protrusion		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Joint stiffness	Additional description: Joint stiffness		
subjects affected / exposed	3 / 642 (0.47%)	6 / 430 (1.40%)	3 / 639 (0.47%)
occurrences (all)	7	9	6
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed	8 / 642 (1.25%)	4 / 430 (0.93%)	2 / 639 (0.31%)
occurrences (all)	8	4	2
Ligament pain	Additional description: Ligament pain		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Limb discomfort	Additional description: Limb discomfort		
subjects affected / exposed	0 / 642 (0.00%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	0	2	1
Limb mass	Additional description: Limb mass		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Mobility decreased	Additional description: Mobility decreased		

subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	25 / 642 (3.89%)	10 / 430 (2.33%)	35 / 639 (5.48%)
occurrences (all)	38	17	59
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	4 / 642 (0.62%)	2 / 430 (0.47%)	4 / 639 (0.63%)
occurrences (all)	4	2	4
Musculoskeletal discomfort	Additional description: Musculoskeletal discomfort		
subjects affected / exposed	2 / 642 (0.31%)	4 / 430 (0.93%)	2 / 639 (0.31%)
occurrences (all)	2	4	2
Musculoskeletal disorder	Additional description: Musculoskeletal disorder		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	4 / 642 (0.62%)	4 / 430 (0.93%)	0 / 639 (0.00%)
occurrences (all)	4	4	0
Musculoskeletal stiffness	Additional description: Musculoskeletal stiffness		
subjects affected / exposed	2 / 642 (0.31%)	2 / 430 (0.47%)	2 / 639 (0.31%)
occurrences (all)	2	2	2
Myalgia	Additional description: Myalgia		
subjects affected / exposed	19 / 642 (2.96%)	10 / 430 (2.33%)	16 / 639 (2.50%)
occurrences (all)	24	13	18
Myositis	Additional description: Myositis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	2
Neck pain	Additional description: Neck pain		
subjects affected / exposed	2 / 642 (0.31%)	5 / 430 (1.16%)	6 / 639 (0.94%)
occurrences (all)	2	5	7
Osteoarthritis	Additional description: Osteoarthritis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Pain in extremity	Additional description: Pain in extremity		

subjects affected / exposed	27 / 642 (4.21%)	21 / 430 (4.88%)	24 / 639 (3.76%)
occurrences (all)	33	27	33
Pain in jaw	Additional description: Pain in jaw		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	1	1	1
Pain of skin	Additional description: Pain of skin		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Periarthritis	Additional description: Periarthritis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	2	1
Plantar fasciitis	Additional description: Plantar fasciitis		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	1	3	1
Polyarthritis	Additional description: Polyarthritis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Polymyalgia rheumatica	Additional description: Polymyalgia rheumatica		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	3	0	0
Rheumatoid arthritis	Additional description: Rheumatoid arthritis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Synovial cyst	Additional description: Synovial cyst		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Tendon pain	Additional description: Tendon pain		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Tendonitis	Additional description: Tendonitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	1	0	1
Tenosynovitis	Additional description: Tenosynovitis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Trigger finger	Additional description: Trigger finger		

subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Infections and infestations			
Abscess	Additional description: Abscess		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	3 / 639 (0.47%) 4
Anal abscess	Additional description: Anal abscess		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	3 / 639 (0.47%) 6
Balanitis candida	Additional description: Balanitis candida		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Bronchiolitis	Additional description: Bronchiolitis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Candida infection	Additional description: Candida infection		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	2 / 430 (0.47%) 2	1 / 639 (0.16%) 1
Cardiac infection	Additional description: Cardiac infection		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed occurrences (all)	5 / 642 (0.78%) 6	0 / 430 (0.00%) 0	3 / 639 (0.47%) 3
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Cystitis	Additional description: Cystitis		
subjects affected / exposed occurrences (all)	3 / 642 (0.47%) 3	5 / 430 (1.16%) 5	0 / 639 (0.00%) 0
Diverticulitis	Additional description: Diverticulitis		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1

Ear infection subjects affected / exposed occurrences (all)	Additional description: Ear infection		
	3 / 642 (0.47%) 3	0 / 430 (0.00%) 0	3 / 639 (0.47%) 3
Ear infection fungal subjects affected / exposed occurrences (all)	Additional description: Ear infection fungal		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Epididymitis subjects affected / exposed occurrences (all)	Additional description: Epididymitis		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 2
Erysipelas subjects affected / exposed occurrences (all)	Additional description: Erysipelas		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Folliculitis subjects affected / exposed occurrences (all)	Additional description: Folliculitis		
	11 / 642 (1.71%) 15	1 / 430 (0.23%) 1	6 / 639 (0.94%) 8
Fungal infection subjects affected / exposed occurrences (all)	Additional description: Fungal infection		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	2 / 639 (0.31%) 2
Furuncle subjects affected / exposed occurrences (all)	Additional description: Furuncle		
	3 / 642 (0.47%) 4	1 / 430 (0.23%) 1	7 / 639 (1.10%) 9
Gastric infection subjects affected / exposed occurrences (all)	Additional description: Gastric infection		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	Additional description: Gastroenteritis		
	3 / 642 (0.47%) 3	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Gastroenteritis viral subjects affected / exposed occurrences (all)	Additional description: Gastroenteritis viral		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Genital candidiasis subjects affected / exposed occurrences (all)	Additional description: Genital candidiasis		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Gingivitis subjects affected / exposed occurrences (all)	Additional description: Gingivitis		
	4 / 642 (0.62%) 4	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1

Groin abscess subjects affected / exposed occurrences (all)	Additional description: Groin abscess		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Groin infection subjects affected / exposed occurrences (all)	Additional description: Groin infection		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Helicobacter infection subjects affected / exposed occurrences (all)	Additional description: Helicobacter infection		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Herpes virus infection subjects affected / exposed occurrences (all)	Additional description: Herpes virus infection		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Herpes zoster subjects affected / exposed occurrences (all)	Additional description: Herpes zoster		
	3 / 642 (0.47%) 3	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Hordeolum subjects affected / exposed occurrences (all)	Additional description: Hordeolum		
	2 / 642 (0.31%) 2	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Infection subjects affected / exposed occurrences (all)	Additional description: Infection		
	0 / 642 (0.00%) 0	3 / 430 (0.70%) 3	4 / 639 (0.63%) 4
Influenza subjects affected / exposed occurrences (all)	Additional description: Influenza		
	3 / 642 (0.47%) 3	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Labyrinthitis subjects affected / exposed occurrences (all)	Additional description: Labyrinthitis		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Localised infection subjects affected / exposed occurrences (all)	Additional description: Localised infection		
	1 / 642 (0.16%) 1	2 / 430 (0.47%) 2	2 / 639 (0.31%) 2
Lower respiratory tract infection subjects affected / exposed occurrences (all)	Additional description: Lower respiratory tract infection		
	9 / 642 (1.40%) 11	13 / 430 (3.02%) 15	17 / 639 (2.66%) 17
Nail infection subjects affected / exposed occurrences (all)	Additional description: Nail infection		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0

Nasopharyngitis subjects affected / exposed occurrences (all)	Additional description: Nasopharyngitis		
	8 / 642 (1.25%) 9	11 / 430 (2.56%) 13	7 / 639 (1.10%) 7
Onychomycosis subjects affected / exposed occurrences (all)	Additional description: Onychomycosis		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Oral candidiasis subjects affected / exposed occurrences (all)	Additional description: Oral candidiasis		
	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Oral herpes subjects affected / exposed occurrences (all)	Additional description: Oral herpes		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Paronychia subjects affected / exposed occurrences (all)	Additional description: Paronychia		
	1 / 642 (0.16%) 3	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Periodontitis subjects affected / exposed occurrences (all)	Additional description: Periodontitis		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Pharyngitis subjects affected / exposed occurrences (all)	Additional description: Pharyngitis		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	Additional description: Pneumonia		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Pustule subjects affected / exposed occurrences (all)	Additional description: Pustule		
	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	3 / 639 (0.47%) 5
Respiratory tract infection subjects affected / exposed occurrences (all)	Additional description: Respiratory tract infection		
	3 / 642 (0.47%) 3	1 / 430 (0.23%) 1	2 / 639 (0.31%) 2
Rhinitis subjects affected / exposed occurrences (all)	Additional description: Rhinitis		
	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	2 / 639 (0.31%) 5
Sinusitis subjects affected / exposed occurrences (all)	Additional description: Sinusitis		
	3 / 642 (0.47%) 4	1 / 430 (0.23%) 1	2 / 639 (0.31%) 2

Skin infection subjects affected / exposed occurrences (all)	Additional description: Skin infection		
	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Subcutaneous abscess subjects affected / exposed occurrences (all)	Additional description: Subcutaneous abscess		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Tetanus subjects affected / exposed occurrences (all)	Additional description: Tetanus		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Tinea pedis subjects affected / exposed occurrences (all)	Additional description: Tinea pedis		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Tonsillitis subjects affected / exposed occurrences (all)	Additional description: Tonsillitis		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Tooth abscess subjects affected / exposed occurrences (all)	Additional description: Tooth abscess		
	4 / 642 (0.62%) 4	1 / 430 (0.23%) 1	2 / 639 (0.31%) 2
Tooth infection subjects affected / exposed occurrences (all)	Additional description: Tooth infection		
	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	2 / 639 (0.31%) 2
Upper respiratory tract infection subjects affected / exposed occurrences (all)	Additional description: Upper respiratory tract infection		
	9 / 642 (1.40%) 9	6 / 430 (1.40%) 7	4 / 639 (0.63%) 4
Urinary tract infection subjects affected / exposed occurrences (all)	Additional description: Urinary tract infection		
	14 / 642 (2.18%) 18	12 / 430 (2.79%) 20	5 / 639 (0.78%) 5
Vaginal infection subjects affected / exposed occurrences (all)	Additional description: Vaginal infection		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Viral infection subjects affected / exposed occurrences (all)	Additional description: Viral infection		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	3 / 639 (0.47%) 3
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	Additional description: Vulvovaginal candidiasis		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1

Vulvovaginitis subjects affected / exposed occurrences (all)	Additional description: Vulvovaginitis		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
	0	2	0
Wound infection subjects affected / exposed occurrences (all)	Additional description: Wound infection		
	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
	2	0	1
Metabolism and nutrition disorders			
Cell death subjects affected / exposed occurrences (all)	Additional description: Cell death		
	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
	1	0	2
Decreased appetite subjects affected / exposed occurrences (all)	Additional description: Decreased appetite		
	42 / 642 (6.54%)	8 / 430 (1.86%)	44 / 639 (6.89%)
	61	10	65
Dehydration subjects affected / exposed occurrences (all)	Additional description: Dehydration		
	2 / 642 (0.31%)	2 / 430 (0.47%)	1 / 639 (0.16%)
	2	2	1
Diabetes mellitus subjects affected / exposed occurrences (all)	Additional description: Diabetes mellitus		
	1 / 642 (0.16%)	2 / 430 (0.47%)	1 / 639 (0.16%)
	1	2	1
Diabetes mellitus (incl subtypes) subjects affected / exposed occurrences (all)	Additional description: Diabetes mellitus (incl subtypes)		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
	1	0	0
Diabetes mellitus inadequate control subjects affected / exposed occurrences (all)	Additional description: Diabetes mellitus inadequate control		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
	0	1	0
Fluid retention subjects affected / exposed occurrences (all)	Additional description: Fluid retention		
	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
	1	1	0
Gout subjects affected / exposed occurrences (all)	Additional description: Gout		
	5 / 642 (0.78%)	4 / 430 (0.93%)	6 / 639 (0.94%)
	6	4	13
Hypercalcaemia subjects affected / exposed occurrences (all)	Additional description: Hypercalcaemia		
	0 / 642 (0.00%)	3 / 430 (0.70%)	1 / 639 (0.16%)
	0	5	1
Hypercholesterolaemia	Additional description: Hypercholesterolaemia		

subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	4	9	0
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 642 (0.16%)	3 / 430 (0.70%)	1 / 639 (0.16%)
occurrences (all)	1	5	4
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	1 / 642 (0.16%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	1	1	2
Hyperlipidaemia	Additional description: Hyperlipidaemia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	3
Hypertriglyceridaemia	Additional description: Hypertriglyceridaemia		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Hypoglycaemia	Additional description: Hypoglycaemia		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	3 / 642 (0.47%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	3	1	1
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	5	1	4
Type 2 diabetes mellitus	Additional description: Type 2 diabetes mellitus		
subjects affected / exposed	2 / 642 (0.31%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	2	0	0
Vitamin B12 deficiency	Additional description: Vitamin B12 deficiency		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency	Additional description: Vitamin D deficiency		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2017	<p>Based on the external results and the fact that SORCE was the only trial investigating longer duration of therapy, the following change to the SORCE analysis plan were proposed and approved. The decision to change the analysis plan was made without knowledge of the SORCE data; none of the SORCE TMG members, other than the primary trial statistician, were aware of any developing outcome data, nor were any members of the TSC. These two committees – without the primary trial statistician – made the decision to alter the main aims of the trial.</p> <p>SORCE's new aims were to answer the following questions:</p> <p>(i) Does up to three years of treatment with sorafenib increase DFS compared with placebo: a comparison of Arm C vs Arm A?</p> <p>(ii) If the answer to question (i) is yes, does up to one year of sorafenib (Arm B) increase DFS compared to placebo (Arm A)?</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

N/A

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/33052759>