



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 categorial			
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			
Aortic stenosis	Additional description: 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	Additional description: Cholecystectomy		
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	Additional description: Adverse drug reaction		
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	Additional description: Drug hypersensitivity		
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	Additional description: Asthma		
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	Additional description: Confusional state		
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
Additional description: Blindness			
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
Additional description: Eye disorder			
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
Additional description: Retinal vein occlusion			
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
Additional description: Retinal vein thrombosis			
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
Additional description: Ulcerative keratitis			
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
Additional description: Abdominal pain			
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	Additional description: Cholecystitis		
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	Additional description: Angioedema		
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	Additional description: Hypothalamo-pituitary disorder		
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	Additional description: Arthralgia		
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	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	Additional description: Dehydration		
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		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	2	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 (all)	0	0	1
Pituitary tumour benign	Additional description: Pituitary tumour benign		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	2
Prostate cancer	Additional description: Prostate cancer		
subjects affected / exposed	3 / 642 (0.47%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	3	3	0
Second primary malignancy	Additional description: Second primary malignancy		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	1	0	2
Skin papilloma	Additional description: Skin papilloma		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	2 / 639 (0.31%)
occurrences (all)	0	1	2
Squamous cell carcinoma	Additional description: Squamous cell carcinoma		
subjects affected / exposed	2 / 642 (0.31%)	1 / 430 (0.23%)	5 / 639 (0.78%)
occurrences (all)	2	1	9
Vascular disorders			
Aneurysm	Additional description: Aneurysm		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Arterial spasm	Additional description: Arterial spasm		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	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 (all)	0	0	1
Arteriosclerosis	Additional description: Arteriosclerosis		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Deep vein thrombosis	Additional description: Deep vein thrombosis		

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

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

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

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

subjects affected / exposed occurrences (all)	3 / 642 (0.47%) 3	2 / 430 (0.47%) 2	1 / 639 (0.16%) 3
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	2 / 639 (0.31%) 4
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed occurrences (all)	3 / 642 (0.47%) 3	4 / 430 (0.93%) 6	2 / 639 (0.31%) 2
Malaise	Additional description: Malaise		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	3 / 430 (0.70%) 3	0 / 639 (0.00%) 0
Mucosal dryness	Additional description: Mucosal dryness		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Mucosal haemorrhage	Additional description: Mucosal haemorrhage		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed occurrences (all)	35 / 642 (5.45%) 54	12 / 430 (2.79%) 15	44 / 639 (6.89%) 67
Mucosal pain	Additional description: Mucosal pain		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Mucositis	Additional description: Mucositis		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed occurrences (all)	14 / 642 (2.18%) 19	8 / 430 (1.86%) 11	4 / 639 (0.63%) 5
Oedema	Additional description: Oedema		
subjects affected / exposed occurrences (all)	3 / 642 (0.47%) 3	3 / 430 (0.70%) 3	2 / 639 (0.31%) 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	Additional description: Breast mass		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Breast pain	Additional description: Breast pain		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Breast swelling	Additional description: Breast swelling		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Breast tenderness	Additional description: Breast tenderness		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Erectile dysfunction	Additional description: Erectile dysfunction		
	3 / 642 (0.47%) 4	4 / 430 (0.93%) 4	7 / 639 (1.10%) 14
Genital pain	Additional description: Genital pain		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Gynaecomastia	Additional description: Gynaecomastia		
	2 / 642 (0.31%) 3	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Hydrocele	Additional description: Hydrocele		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Menorrhagia	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 occurrences (all)	2 / 642 (0.31%) 2	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Nipple enlargement	Additional description: Nipple enlargement		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 2	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Nipple disorder	Additional description: Nipple disorder		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Nipple pain	Additional description: Nipple pain		
subjects affected / exposed occurrences (all)	12 / 642 (1.87%) 12	0 / 430 (0.00%) 0	8 / 639 (1.25%) 10
Orchitis noninfective	Additional description: Orchitis noninfective		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Pelvic pain	Additional description: Pelvic pain		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	3 / 430 (0.70%) 3	0 / 639 (0.00%) 0
Perineal rash	Additional description: Perineal rash		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 2	0 / 639 (0.00%) 0
Perineal erythema	Additional description: Perineal erythema		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Prostatomegaly	Additional description: Prostatomegaly		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Scrotal pain	Additional description: Scrotal pain		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 3	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Testicular mass	Additional description: Testicular mass		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	4 / 430 (0.93%) 5	1 / 639 (0.16%) 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 occurrences (all)	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Rhinitis allergic	Additional description: Rhinitis allergic		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 4
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 3	1 / 430 (0.23%) 1	1 / 639 (0.16%) 2
Sinus congestion	Additional description: Sinus congestion		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Sinus disorder	Additional description: Sinus disorder		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 2
Sleep apnoea syndrome	Additional description: Sleep apnoea syndrome		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 3	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Sputum discoloured	Additional description: Sputum discoloured		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Throat irritation	Additional description: Throat irritation		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 2	1 / 639 (0.16%) 1
Psychiatric disorders	Additional description: Abnormal dreams		
Abnormal dreams subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Agitation	Additional description: Agitation		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 2	1 / 639 (0.16%) 1
Anger	Additional description: Anger		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1

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

Mood swings	Additional description: Mood swings		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Nightmare	Additional description: Nightmare		
subjects affected / exposed	1 / 642 (0.16%)	2 / 430 (0.47%)	0 / 639 (0.00%)
occurrences (all)	1	2	0
Personality change	Additional description: Personality change		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Psychotic disorder	Additional description: Psychotic disorder		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Sleep disorder	Additional description: Sleep disorder		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Tearfulness	Additional description: Tearfulness		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Investigations	Additional description: Activated partial thromboplastin time prolonged		
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Adjusted calcium	Additional description: Adjusted calcium		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase abnormal	Additional description: Alanine aminotransferase abnormal		
subjects affected / exposed	2 / 642 (0.31%)	2 / 430 (0.47%)	1 / 639 (0.16%)
occurrences (all)	3	3	1
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	16 / 642 (2.49%)	5 / 430 (1.16%)	19 / 639 (2.97%)
occurrences (all)	20	11	27
Amylase abnormal	Additional description: Amylase abnormal		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	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 occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Blood creatine phosphokinase increased	Additional description: Blood creatine phosphokinase increased		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 5	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Blood creatinine abnormal	Additional description: Blood creatinine abnormal		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	2 / 430 (0.47%) 5	3 / 639 (0.47%) 3
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed occurrences (all)	28 / 642 (4.36%) 44	28 / 430 (6.51%) 49	18 / 639 (2.82%) 27
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	2 / 639 (0.31%) 3
Blood iron decreased	Additional description: Blood iron decreased		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 2	0 / 639 (0.00%) 0
Blood lactate dehydrogenase abnormal	Additional description: Blood lactate dehydrogenase abnormal		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	0 / 639 (0.00%) 0
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		
subjects affected / exposed occurrences (all)	4 / 642 (0.62%) 5	4 / 430 (0.93%) 5	3 / 639 (0.47%) 5
Blood phosphorus abnormal	Additional description: Blood phosphorus abnormal		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Blood phosphorus decreased	Additional description: Blood phosphorus decreased		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	4 / 639 (0.63%) 4
Blood potassium increased	Additional description: Blood potassium increased		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	3 / 430 (0.70%) 4	8 / 639 (1.25%) 10
Blood test abnormal	Additional description: Blood test abnormal		

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

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

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

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

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

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

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

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

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

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

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

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

Eye pruritus	Additional description: Eye pruritus		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Eye swelling	Additional description: Eye swelling		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	1	0	2
Eyelid cyst	Additional description: Eyelid cyst		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Eyelid irritation	Additional description: Eyelid irritation		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema	Additional description: Eyelid oedema		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Foreign body sensation in eyes	Additional description: Foreign body sensation in eyes		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Glaucoma	Additional description: Glaucoma		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	1 / 639 (0.16%)
occurrences (all)	0	0	1
Iritis	Additional description: Iritis		
subjects affected / exposed	0 / 642 (0.00%)	0 / 430 (0.00%)	2 / 639 (0.31%)
occurrences (all)	0	0	2
Keratitis	Additional description: Keratitis		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	0 / 642 (0.00%)	1 / 430 (0.23%)	1 / 639 (0.16%)
occurrences (all)	0	1	1
Ocular hyperaemia	Additional description: Ocular hyperaemia		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	0
Periorbital swelling	Additional description: Periorbital swelling		
subjects affected / exposed	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
occurrences (all)	1	0	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
Retinal detachment subjects affected / exposed occurrences (all)	Additional description: Retinal detachment		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Retinal haemorrhage subjects affected / exposed occurrences (all)	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
Abdominal distension subjects affected / exposed occurrences (all)	Additional description: Abdominal distension		
	9 / 642 (1.40%) 10	8 / 430 (1.86%) 14	6 / 639 (0.94%) 6
Abdominal hernia subjects affected / exposed occurrences (all)	Additional description: Abdominal hernia		
	0 / 642 (0.00%) 0	2 / 430 (0.47%) 6	0 / 639 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	Additional description: Abdominal pain		
	39 / 642 (6.07%) 49	32 / 430 (7.44%) 50	53 / 639 (8.29%) 85
Abdominal pain lower subjects affected / exposed occurrences (all)	Additional description: Abdominal pain lower		
	2 / 642 (0.31%) 2	5 / 430 (1.16%) 8	4 / 639 (0.63%) 5
Abdominal pain upper	Additional description: Abdominal pain upper		

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

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

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

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

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

subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed occurrences (all)	60 / 642 (9.35%) 92	17 / 430 (3.95%) 32	63 / 639 (9.86%) 105
Swollen tongue	Additional description: Swollen tongue		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Tongue discolouration	Additional description: Tongue discolouration		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Tongue ulceration	Additional description: Tongue ulceration		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Tongue dry	Additional description: Tongue dry		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Tooth disorder	Additional description: Tooth disorder		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Toothache	Additional description: Toothache		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 4	2 / 430 (0.47%) 2	4 / 639 (0.63%) 9
Umbilical hernia	Additional description: Umbilical hernia		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Vomiting	Additional description: Vomiting		
subjects affected / exposed occurrences (all)	26 / 642 (4.05%) 32	10 / 430 (2.33%) 12	26 / 639 (4.07%) 39
Hepatobiliary disorders			
Biliary colic	Additional description: Biliary colic		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Cholecystitis	Additional description: Cholecystitis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 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 occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Dermatitis exfoliative generalised	Additional description: Dermatitis exfoliative generalised		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 2	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Dry skin	Additional description: Dry skin		
subjects affected / exposed occurrences (all)	46 / 642 (7.17%) 71	25 / 430 (5.81%) 55	39 / 639 (6.10%) 70
Dyshidrotic eczema	Additional description: Dyshidrotic eczema		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Eczema	Additional description: Eczema		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 2	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Eczema asteatotic	Additional description: Eczema asteatotic		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Erythema	Additional description: Erythema		
subjects affected / exposed occurrences (all)	18 / 642 (2.80%) 23	5 / 430 (1.16%) 5	12 / 639 (1.88%) 17
Furuncle	Additional description: Furuncle		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Haemorrhage subcutaneous	Additional description: Haemorrhage subcutaneous		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Hair colour changes	Additional description: Hair colour changes		
subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	0 / 430 (0.00%) 0	3 / 639 (0.47%) 4
Hair growth abnormal	Additional description: Hair growth abnormal		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	2 / 639 (0.31%) 2
Hair texture abnormal	Additional description: Hair texture abnormal		
subjects affected / exposed occurrences (all)	5 / 642 (0.78%) 5	1 / 430 (0.23%) 1	3 / 639 (0.47%) 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 subjects affected / exposed occurrences (all)	Additional description: Scar pain		
	12 / 642 (1.87%) 13	21 / 430 (4.88%) 34	13 / 639 (2.03%) 16
Skin atrophy subjects affected / exposed occurrences (all)	Additional description: Skin atrophy		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Skin depigmentation subjects affected / exposed occurrences (all)	Additional description: Skin depigmentation		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Skin discolouration subjects affected / exposed occurrences (all)	Additional description: Skin discolouration		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Skin disorder subjects affected / exposed occurrences (all)	Additional description: Skin disorder		
	2 / 642 (0.31%) 2	3 / 430 (0.70%) 3	5 / 639 (0.78%) 5
Skin exfoliation subjects affected / exposed occurrences (all)	Additional description: Skin exfoliation		
	1 / 642 (0.16%) 2	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Skin fissures subjects affected / exposed occurrences (all)	Additional description: Skin fissures		
	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Skin hypertrophy subjects affected / exposed occurrences (all)	Additional description: Skin hypertrophy		
	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Skin irritation subjects affected / exposed occurrences (all)	Additional description: Skin irritation		
	4 / 642 (0.62%) 7	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Skin lesion subjects affected / exposed occurrences (all)	Additional description: Skin lesion		
	4 / 642 (0.62%) 6	1 / 430 (0.23%) 1	4 / 639 (0.63%) 5
Skin mass subjects affected / exposed occurrences (all)	Additional description: Skin mass		
	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	2 / 639 (0.31%) 2
Skin papilloma subjects affected / exposed occurrences (all)	Additional description: Skin papilloma		
	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 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 occurrences (all)	3 / 642 (0.47%) 3	3 / 430 (0.70%) 7	4 / 639 (0.63%) 5
Hypertonic bladder	Additional description: Hypertonic bladder		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Lower urinary tract symptoms	Additional description: Lower urinary tract symptoms		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Micturition urgency	Additional description: Micturition urgency		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 5	1 / 430 (0.23%) 1	2 / 639 (0.31%) 2
Nephrolithiasis	Additional description: Nephrolithiasis		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Nocturia	Additional description: Nocturia		
subjects affected / exposed occurrences (all)	5 / 642 (0.78%) 7	6 / 430 (1.40%) 18	3 / 639 (0.47%) 3
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed occurrences (all)	4 / 642 (0.62%) 5	5 / 430 (1.16%) 9	3 / 639 (0.47%) 3
Polyuria	Additional description: Polyuria		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Proteinuria	Additional description: Proteinuria		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	2 / 430 (0.47%) 2	2 / 639 (0.31%) 2
Renal colic	Additional description: Renal colic		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Renal failure	Additional description: Renal failure		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 3	0 / 639 (0.00%) 0
Renal pain	Additional description: Renal pain		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	4 / 430 (0.93%) 5	2 / 639 (0.31%) 2
Renal vein occlusion	Additional description: Renal vein occlusion		

subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Urethral haemorrhage	Additional description: Urethral haemorrhage		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Urethral stenosis	Additional description: Urethral stenosis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Urinary incontinence	Additional description: Urinary incontinence		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Urinary tract disorder	Additional description: Urinary tract disorder		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Urine abnormality	Additional description: Urine abnormality		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Endocrine disorders	Additional description: Endocrine disorders		
Hyperparathyroidism	Additional description: Hyperparathyroidism		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 3	0 / 639 (0.00%) 0
Hyperthyroidism	Additional description: Hyperthyroidism		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 2	0 / 639 (0.00%) 0
Hypogonadism	Additional description: Hypogonadism		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 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			
Abdominal pain upper subjects affected / exposed occurrences (all)	Additional description: Abdominal pain upper		
	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 occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Bursitis	Additional description: Bursitis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Fibromyalgia	Additional description: Fibromyalgia		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Fistula	Additional description: Fistula		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Flank pain	Additional description: Flank pain		
subjects affected / exposed occurrences (all)	6 / 642 (0.93%) 8	12 / 430 (2.79%) 17	8 / 639 (1.25%) 12
Groin pain	Additional description: Groin pain		
subjects affected / exposed occurrences (all)	6 / 642 (0.93%) 7	7 / 430 (1.63%) 11	3 / 639 (0.47%) 3
Intervertebral disc protrusion	Additional description: Intervertebral disc protrusion		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Joint stiffness	Additional description: Joint stiffness		
subjects affected / exposed occurrences (all)	3 / 642 (0.47%) 7	6 / 430 (1.40%) 9	3 / 639 (0.47%) 6
Joint swelling	Additional description: Joint swelling		
subjects affected / exposed occurrences (all)	8 / 642 (1.25%) 8	4 / 430 (0.93%) 4	2 / 639 (0.31%) 2
Ligament pain	Additional description: Ligament pain		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Limb discomfort	Additional description: Limb discomfort		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	2 / 430 (0.47%) 2	1 / 639 (0.16%) 1
Limb mass	Additional description: Limb mass		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 2	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Mobility decreased	Additional description: Mobility decreased		

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

subjects affected / exposed occurrences (all)	27 / 642 (4.21%) 33	21 / 430 (4.88%) 27	24 / 639 (3.76%) 33
Pain in jaw	Additional description: Pain in jaw		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	1 / 639 (0.16%) 1
Pain of skin	Additional description: Pain of skin		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Periarthritis	Additional description: Periarthritis		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 2	1 / 639 (0.16%) 1
Plantar fasciitis	Additional description: Plantar fasciitis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	2 / 430 (0.47%) 3	1 / 639 (0.16%) 1
Polyarthritis	Additional description: Polyarthritis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Polymyalgia rheumatica	Additional description: Polymyalgia rheumatica		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 3	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Rheumatoid arthritis	Additional description: Rheumatoid arthritis		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Synovial cyst	Additional description: Synovial cyst		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Tendon pain	Additional description: Tendon pain		
subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Tendonitis	Additional description: Tendonitis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Tenosynovitis	Additional description: Tenosynovitis		
subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 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			
Additional description: Abscess			
Abscess subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	3 / 639 (0.47%) 4
Additional description: Anal abscess			
Anal abscess subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	3 / 639 (0.47%) 6
Additional description: Balanitis candida			
Balanitis candida subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Additional description: Bronchiolitis			
Bronchiolitis subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	0 / 430 (0.00%) 0	0 / 639 (0.00%) 0
Additional description: Bronchitis			
Bronchitis subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Additional description: Candida infection			
Candida infection subjects affected / exposed occurrences (all)	1 / 642 (0.16%) 1	2 / 430 (0.47%) 2	1 / 639 (0.16%) 1
Additional description: Cardiac infection			
Cardiac infection subjects affected / exposed occurrences (all)	0 / 642 (0.00%) 0	0 / 430 (0.00%) 0	1 / 639 (0.16%) 1
Additional description: Cellulitis			
Cellulitis subjects affected / exposed occurrences (all)	5 / 642 (0.78%) 6	0 / 430 (0.00%) 0	3 / 639 (0.47%) 3
Additional description: Conjunctivitis			
Conjunctivitis subjects affected / exposed occurrences (all)	2 / 642 (0.31%) 2	1 / 430 (0.23%) 1	0 / 639 (0.00%) 0
Additional description: Cystitis			
Cystitis subjects affected / exposed occurrences (all)	3 / 642 (0.47%) 3	5 / 430 (1.16%) 5	0 / 639 (0.00%) 0
Additional description: Diverticulitis			
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	Additional description: Vulvovaginitis		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	0	2	0
Wound infection	Additional description: Wound infection		
	2 / 642 (0.31%)	0 / 430 (0.00%)	1 / 639 (0.16%)
subjects affected / exposed			
occurrences (all)	2	0	1
Metabolism and nutrition disorders			
Cell death	Additional description: Cell death		
	1 / 642 (0.16%)	0 / 430 (0.00%)	2 / 639 (0.31%)
subjects affected / exposed			
occurrences (all)	1	0	2
Decreased appetite	Additional description: Decreased appetite		
	42 / 642 (6.54%)	8 / 430 (1.86%)	44 / 639 (6.89%)
subjects affected / exposed			
occurrences (all)	61	10	65
Dehydration	Additional description: Dehydration		
	2 / 642 (0.31%)	2 / 430 (0.47%)	1 / 639 (0.16%)
subjects affected / exposed			
occurrences (all)	2	2	1
Diabetes mellitus	Additional description: Diabetes mellitus		
	1 / 642 (0.16%)	2 / 430 (0.47%)	1 / 639 (0.16%)
subjects affected / exposed			
occurrences (all)	1	2	1
Diabetes mellitus (incl subtypes)	Additional description: Diabetes mellitus (incl subtypes)		
	1 / 642 (0.16%)	0 / 430 (0.00%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	1	0	0
Diabetes mellitus inadequate control	Additional description: Diabetes mellitus inadequate control		
	0 / 642 (0.00%)	1 / 430 (0.23%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	0	1	0
Fluid retention	Additional description: Fluid retention		
	1 / 642 (0.16%)	1 / 430 (0.23%)	0 / 639 (0.00%)
subjects affected / exposed			
occurrences (all)	1	1	0
Gout	Additional description: Gout		
	5 / 642 (0.78%)	4 / 430 (0.93%)	6 / 639 (0.94%)
subjects affected / exposed			
occurrences (all)	6	4	13
Hypercalcaemia	Additional description: Hypercalcaemia		
	0 / 642 (0.00%)	3 / 430 (0.70%)	1 / 639 (0.16%)
subjects affected / exposed			
occurrences (all)	0	5	1
Hypercholesterolaemia	Additional description: Hypercholesterolaemia		

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