



## Clinical trial results:

**International Breast Cancer Intervention Study II (DCIS). An international multi-centre trial of tamoxifen v anastrozole in post-menopausal women with ductal carcinoma in situ.**

### Summary

EudraCT number	2004-003992-35
Trial protocol	SE
Global end of trial date	31 May 2021

### Results information

Result version number	v1 (current)
This version publication date	12 May 2022
First version publication date	12 May 2022

### Trial information

#### Trial identification

Sponsor protocol code	MREC02/8/71
-----------------------	-------------

#### Additional study identifiers

ISRCTN number	ISRCTN37546358
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Queen Mary University London
Sponsor organisation address	Wolfson Institute of Population Health, London, United Kingdom, EC1M 6BQ
Public contact	Professor Jack Cuzick, Queen Mary University London, j.cuzick@qmul.ac.uk
Scientific contact	Professor Jack Cuzick, Queen Mary University London, j.cuzick@qmul.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	31 May 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 May 2021
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To determine if anastrozole is at least as effective as tamoxifen in local control and prevention of contralateral disease in women with locally excised ER or PgR+ve DCIS and to compare side effect profiles of tamoxifen and anastrozole.

Protection of trial subjects:

Eligibility criteria were risk-based, varied by age, and defined in the protocol to ensure protection of participants. Participants were informed of potential side-effects prior to study entry and if new side-effects were added to the Summary of Product Characteristics (SmPC) after randomisation, women were informed at their next clinic appointment. Women were informed of their right to withdraw at any point.

Only post-menopausal women diagnosed with locally excised, hormone-receptor-positive DCIS were eligible. Women aged 60 without a uterus were eligible if they had FSH levels >30 IU/L and if taking HRT, an 8 week wash-out period was required prior to a FSH test being performed. Due to potential concerns over the effects of the trial interventions on pre-existing conditions associated with low bone mineral density, women with osteoporosis were excluded and a DXA scan and spinal radiograph within the last two years was required prior to randomisation.

Advice on maintaining healthy bones was offered to women in the trial. Treatment with bisphosphonates was considered where necessary. If serious menopausal symptoms developed during treatment, management followed a protocolised approach including details on when to reduce dosing of the trial intervention. Circumstances which indicated cessation of the IMP were listed in the protocol. A codebreak procedure to unblind clinicians and participants was active throughout the study. Adverse events were collected and reviewed regularly by the Trial team and Steering Committee.

Background therapy: -

Evidence for comparator:

IBIS-II (DCIS) is designed to continue the work started in IBIS-I in determining whether a chemo preventive strategy towards breast cancer is beneficial. IBIS-I was set up to investigate the use of tamoxifen as a preventive agent for women with moderate to increased risk of getting breast cancer. IBIS-II (DCIS) is a randomized double blind control trial which will compare tamoxifen versus anastrozole in women with locally excised ER or PgR positive Ductal Carcinoma In-Situ (ER or PgR+ve DCIS).

Actual start date of recruitment	03 March 2003
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	United Kingdom: 889
Country: Number of subjects enrolled	Italy: 323

Country: Number of subjects enrolled	Australia: 168
Country: Number of subjects enrolled	Switzerland: 45
Country: Number of subjects enrolled	Belgium: 104
Country: Number of subjects enrolled	Chile: 17
Country: Number of subjects enrolled	Finland: 7
Country: Number of subjects enrolled	Ireland: 78
Country: Number of subjects enrolled	France: 426
Country: Number of subjects enrolled	Germany: 779
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Malta: 4
Country: Number of subjects enrolled	New Zealand: 10
Country: Number of subjects enrolled	Turkey: 15
Country: Number of subjects enrolled	Austria: 90
Country: Number of subjects enrolled	India: 2
Worldwide total number of subjects	2980
EEA total number of subjects	1834

Notes:

<b>Subjects enrolled per age group</b>	
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)	2310
From 65 to 84 years	670
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Between March 3, 2003, and Feb 8, 2012, women who had been diagnosed with locally excised, hormone-receptor-positive DCIS were recruited from 236 centres in 17 countries (Sweden, UK, Italy, Australia, Switzerland, Belgium, Chile, Finland, Ireland, France, Germany, Hungary, Malta, New Zealand, Turkey, Austria, India).

### Pre-assignment

Screening details:

Potentially eligible women were given an information sheet. Informed consent was taken from interested patients and pre-randomisation eligibility assessment was conducted. Eligibility criteria were clearly listed in the protocol.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Anastrozole

Arm description: -

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

Dosage and administration details:

Anastrozole 1mg + Tamoxifen placebo. All treatment will be on a daily basis for 5 years and all women will take 2 tablets/day. One will contain tamoxifen or placebo. The second tablet will contain either anastrozole or placebo. Tablets will be supplied in numbered light-proof containers containing a 6-month supply. Each container will have extra tablets to allow for some delay in the next appointment.

<b>Arm title</b>	Tamoxifen
------------------	-----------

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Tamoxifen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tamoxifen 20mg + Anastrozole placebo. All treatment will be on a daily basis for 5 years and all women will take 2 tablets/day. One will contain tamoxifen or placebo. The second tablet will contain either anastrozole or placebo. Tablets will be supplied in numbered light-proof containers containing a 6-month supply. Each container will have extra tablets to allow for some delay in the next appointment.

<b>Number of subjects in period 1</b>	Anastrozole	Tamoxifen
Started	1471	1509
Completed	1449	1489
Not completed	22	20
Consent withdrawn by subject	22	20

## Baseline characteristics

### Reporting groups

Reporting group title	Anastrozole
Reporting group description: -	
Reporting group title	Tamoxifen
Reporting group description: -	

Reporting group values	Anastrozole	Tamoxifen	Total
Number of subjects	1471	1509	2980
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)	1139	1171	2310
From 65-84 years	332	338	670
85 years and over	0	0	0
Age continuous Units: years			
median	60.4	60.3	
inter-quartile range (Q1-Q3)	56.4 to 64.7	55.8 to 64.5	-
Gender categorical Units: Subjects			
Female	1471	1509	2980
Male	0	0	0

## End points

### End points reporting groups

Reporting group title	Anastrozole
Reporting group description: -	
Reporting group title	Tamoxifen
Reporting group description: -	

### Primary: Breast cancer recurrence, including recurrent DCIS and new contralateral tumours

End point title	Breast cancer recurrence, including recurrent DCIS and new contralateral tumours
End point description:	
End point type	Primary
End point timeframe:	
From 3 March 2003 to 31 May 2021.	

End point values	Anastrozole	Tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1449	1489		
Units: Breast cancer recurrence	103	120		

### Statistical analyses

Statistical analysis title	Univariate Cox Model
Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.14
Variability estimate	Standard deviation
Dispersion value	0.12

<b>Statistical analysis title</b>	Multivariate Cox Model
-----------------------------------	------------------------

Statistical analysis description:

The following baseline characteristics will be included in the Cox proportional hazard models adjusting for baseline covariates for the incidence of breast cancer. The covariates will be included in the models regardless of statistical significance: • Hormone Replacement Therapy (HRT) use • Age • Body Mass Index (BMI) • Use of radiotherapy • Extent of margins • Grade (categorical: low, medium, high)

Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.15
Variability estimate	Standard deviation
Dispersion value	0.12

## Secondary: ER+ breast cancer recurrence, including recurrent DCIS and new contralateral tumours

End point title	ER+ breast cancer recurrence, including recurrent DCIS and new contralateral tumours
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

From 3 March 2003 to 31 May 2021.

<b>End point values</b>	Anastrozole	Tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1449	1489		
Units: ER+ breast cancer recurrence	58	82		

## Statistical analyses



<b>Statistical analysis title</b>	Univariate Cox Model
Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.01
Variability estimate	Standard deviation
Dispersion value	0.12

<b>Statistical analysis title</b>	Multivariate Cox Model
Statistical analysis description:	
The following baseline characteristics will be included in the Cox proportional hazard models adjusting for baseline covariates for the incidence of ER+ breast cancer. The covariates will be included in the models regardless of statistical significance: • Hormone Replacement Therapy (HRT) use • Age • Body Mass Index (BMI) • Use of radiotherapy • Extent of margins • Grade (categorical: low, medium, high)	
Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.09
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.05
Variability estimate	Standard deviation
Dispersion value	0.13

## Secondary: ER- breast cancer recurrence

End point title	ER- breast cancer recurrence
End point description:	
End point type	Secondary
End point timeframe:	
From 3 March 2003 to 31 May 2021.	

<b>End point values</b>	Anastrozole	Tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1449	1489		
Units: ER- breast cancer recurrence	24	15		

## Statistical analyses

<b>Statistical analysis title</b>	Univariate Cox Model
Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	3.12
Variability estimate	Standard deviation
Dispersion value	0.54

<b>Statistical analysis title</b>	Multivariate Cox Model
Statistical analysis description:	
The following baseline characteristics will be included in the Cox proportional hazard models adjusting for baseline covariates for the incidence of ER- breast cancer. The covariates will be included in the models regardless of statistical significance: • Hormone Replacement Therapy (HRT) use • Age • Body Mass Index (BMI) • Use of radiotherapy • Extent of margins • Grade (categorical: low, medium, high)	
Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.84

Variability estimate	Standard deviation
Dispersion value	0.5

## Secondary: Breast cancer mortality

End point title	Breast cancer mortality
End point description:	
End point type	Secondary
End point timeframe:	
From 3 March 2003 to 31 May 2021.	

End point values	Anastrozole	Tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1449	1489		
Units: Breast cancer mortality	3	3		

## Statistical analyses

<b>Statistical analysis title</b>	Univariate Cox Model
Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	5.11
Variability estimate	Standard deviation
Dispersion value	0.84

<b>Statistical analysis title</b>	Multivariate Cox Model
Statistical analysis description:	
The following baseline characteristics will be included in the Cox proportional hazard models adjusting for baseline covariates for the incidence of breast cancer mortality. The covariates will be included in the models regardless of statistical significance: • Hormone Replacement Therapy (HRT) use • Age • Body Mass Index (BMI) • Use of radiotherapy • Extent of margins • Grade (categorical: low, medium, high)	
Comparison groups	Anastrozole v Tamoxifen

Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.93
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	5.36
Variability estimate	Standard deviation
Dispersion value	0.88

### Secondary: Non-breast cancer mortality

End point title	Non-breast cancer mortality
End point description:	
End point type	Secondary
End point timeframe:	
From 3 March 2003 to 31 May 2021.	

End point values	Anastrozole	Tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1449	1489		
Units: Non-breast cancer mortality	59	65		

### Statistical analyses

<b>Statistical analysis title</b>	Univariate Cox Model
Comparison groups	Tamoxifen v Anastrozole
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.32
Variability estimate	Standard deviation
Dispersion value	0.17

<b>Statistical analysis title</b>	Multivariate Cox Model
-----------------------------------	------------------------

Statistical analysis description:

The following baseline characteristics will be included in the Cox proportional hazard models adjusting for baseline covariates for the incidence of non-breast cancer mortality. The covariates will be included in the models regardless of statistical significance: • Hormone Replacement Therapy (HRT) use • Age • Body Mass Index (BMI) • Use of radiotherapy • Extent of margins • Grade (categorical: low, medium, high)

Comparison groups	Anastrozole v Tamoxifen
Number of subjects included in analysis	2938
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.38
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.22
Variability estimate	Standard deviation
Dispersion value	0.16

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From 3 March 2003 to 31 May 2021.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	19
--------------------	----

### Reporting groups

Reporting group title	Anastrozole
-----------------------	-------------

Reporting group description: -

Reporting group title	Tamoxifen
-----------------------	-----------

Reporting group description: -

Serious adverse events	Anastrozole	Tamoxifen	
Total subjects affected by serious adverse events			
subjects affected / exposed	333 / 1449 (22.98%)	371 / 1489 (24.92%)	
number of deaths (all causes)	62	69	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal papilloma of breast			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast angiosarcoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer in situ			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer metastatic			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paget's disease of the breast			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melanocytic naevus			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid adenoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid tumour of the caecum			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			

subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Phaeochromocytoma			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland adenoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anal cancer			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			



subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colorectal cancer			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer metastatic			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric cancer			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal carcinoma			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal neoplasm			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroesophageal cancer			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lip and/or oral cavity cancer			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant palate neoplasm			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant peritoneal neoplasm			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Oral cavity cancer metastatic			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Rectal cancer			
subjects affected / exposed	5 / 1449 (0.35%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rectal cancer metastatic			

subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectosigmoid cancer recurrent			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Salivary gland cancer			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Essential thrombocythaemia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematological malignancy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myeloproliferative disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Focal nodular hyperplasia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cancer			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer metastatic			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hairy cell leukaemia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			

subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mesothelioma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural mesothelioma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural mesothelioma malignant			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to bone			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to lung			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to peritoneum			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Adenoma benign			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	4 / 1449 (0.28%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 4	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant neoplasm of unknown primary site			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic squamous cell carcinoma			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm malignant			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Meningeal neoplasm			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular melanoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple myeloma			

subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 1	0 / 2	
Bladder cancer			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	5 / 1449 (0.35%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign ovarian tumour			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			



subjects affected / exposed	1 / 1449 (0.07%)	6 / 1489 (0.40%)	
occurrences causally related to treatment / all	0 / 1	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cervix carcinoma recurrent			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	1 / 1449 (0.07%)	8 / 1489 (0.54%)	
occurrences causally related to treatment / all	1 / 1	5 / 8	
deaths causally related to treatment / all	0 / 0	0 / 2	
Endometrial cancer metastatic			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endometrial cancer stage I			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial neoplasm			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fallopian tube cancer			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			

subjects affected / exposed	1 / 1449 (0.07%)	7 / 1489 (0.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
Bronchial carcinoma			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Lung adenocarcinoma metastatic			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung cancer metastatic			
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Lung neoplasm			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	8 / 1449 (0.55%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 4	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Small cell lung cancer recurrent			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Small cell lung cancer stage unspecified			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tonsil cancer			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 1449 (0.07%)	5 / 1489 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 1449 (0.07%)	5 / 1489 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
Melanoma recurrent			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angiomyolipoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leiomyoma			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory myofibroblastic tumour			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoma uterus			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arterial stenosis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Infarction			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous insufficiency			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial thrombosis limb			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	5 / 1449 (0.35%)	14 / 1489 (0.94%)	
occurrences causally related to treatment / all	3 / 5	8 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic venous thrombosis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	2 / 1449 (0.14%)	5 / 1489 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			

subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hot flush			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose ulceration			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Bunion operation			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			

subjects affected / exposed	2 / 1449 (0.14%)	5 / 1489 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint arthroplasty			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff repair			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mammoplasty			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve replacement			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac pacemaker insertion			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve replacement			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid operation			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroidectomy			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye operation			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia repair			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicectomy			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colectomy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia repair			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laparotomy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal prolapse repair			



subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystectomy			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma surgery			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal laminectomy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal operation			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hysterectomy			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oophorectomy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oophorectomy bilateral			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingo-oophorectomy bilateral			

subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine dilation and curettage			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine operation			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine tumour excision			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrectomy			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Removal of inert matter from skin or subcutaneous tissue			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scar excision			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin graft			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer surgery			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Debridement			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Elective surgery			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lesion excision			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant tumour excision			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound closure			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery bypass			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac death			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Death			
subjects affected / exposed	14 / 1449 (0.97%)	10 / 1489 (0.67%)	
occurrences causally related to treatment / all	0 / 14	0 / 10	
deaths causally related to treatment / all	0 / 14	0 / 10	
Asthenia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	2 / 1449 (0.14%)	6 / 1489 (0.40%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Fatigue			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pain			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyp			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic mass			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			

subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Breast haematoma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast necrosis			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast pain			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical cyst			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 1449 (0.07%)	6 / 1489 (0.40%)	
occurrences causally related to treatment / all	1 / 1	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			

subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian atrophy			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Female genital tract fistula			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystocele			
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial dysplasia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hyperplasia			
subjects affected / exposed	1 / 1449 (0.07%)	12 / 1489 (0.81%)	
occurrences causally related to treatment / all	0 / 1	6 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial hypertrophy			

subjects affected / exposed	0 / 1449 (0.00%)	5 / 1489 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine atrophy			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 1449 (0.07%)	15 / 1489 (1.01%)	
occurrences causally related to treatment / all	1 / 1	9 / 15	
deaths causally related to treatment / all	0 / 0	0 / 1	
Uterine prolapse			
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterovaginal prolapse			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal prolapse			
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			



subjects affected / exposed	3 / 1449 (0.21%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal polyp			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulvovaginal discomfort			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	5 / 1449 (0.35%)	9 / 1489 (0.60%)	
occurrences causally related to treatment / all	0 / 5	6 / 9	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cough			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal haemorrhage			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nasal septum deviation			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep disorder			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Suicide attempt			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate increased			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigation			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose fluctuation			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthroscopy			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular pressure increased			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Body temperature increased			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystoscopy			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hysteroscopy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Smear cervix abnormal			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Acetabulum fracture			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	10 / 1449 (0.69%)	11 / 1489 (0.74%)	
occurrences causally related to treatment / all	0 / 10	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cartilage injury			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	3 / 1449 (0.21%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	1 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	4 / 1449 (0.28%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	4 / 1449 (0.28%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint sprain			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			



subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus lesion			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	2 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	1 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation fibrosis - lung			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation necrosis			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation pneumonitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	6 / 1449 (0.41%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Head injury			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ligament injury			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			

subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Tendon rupture			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic anuria			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple drug overdose			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dislocation of joint prosthesis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural pulmonary embolism			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound decomposition			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	5 / 1449 (0.35%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block left			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bundle branch block right			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Extrasystoles			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarctioncardial			

subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Angina unstable			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	4 / 1449 (0.28%)	6 / 1489 (0.40%)	
occurrences causally related to treatment / all	1 / 4	2 / 6	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cardiac failure			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Arachnoiditis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem stroke			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			



subjects affected / exposed	4 / 1449 (0.28%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	10 / 1449 (0.69%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	2 / 10	1 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	10 / 1449 (0.69%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	1 / 10	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amnesia			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paresis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Altered state of consciousness			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic hyperosmolar coma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 1449 (0.28%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic nervous system imbalance			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Motor neurone disease			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve compression			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	5 / 1449 (0.35%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract cortical			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular hypertension			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open angle glaucoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye irritation			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papilloedema			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			

subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal vein occlusion			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blindness unilateral			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocoele			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic polyp			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingival hypoplasia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic disorder			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			



subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophagitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Frequent bowel movements			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal discomfort			

subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus of small bowel			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ulcer			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic artery aneurysm			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder polyp			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cirrhosis alcoholic			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cirrhosis			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic cyst			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hydronephrosis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney enlargement			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery thrombosis			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal failure acute			
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal impairment			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral disorder			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incontinence			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mixed incontinence			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress urinary incontinence			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			



subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroiditis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteopenia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in jaw			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sjogren's syndrome			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture nonunion			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			

subjects affected / exposed	5 / 1449 (0.35%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	15 / 1449 (1.04%)	11 / 1489 (0.74%)	
occurrences causally related to treatment / all	3 / 15	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trismus			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spine flattening			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			

subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dupuytren's contracture			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis stenosaurs			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondropathy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast abscess			

subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	5 / 1449 (0.35%)	3 / 1489 (0.20%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail infection			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 1449 (0.35%)	10 / 1489 (0.67%)	
occurrences causally related to treatment / all	0 / 5	0 / 10	
deaths causally related to treatment / all	0 / 1	0 / 2	
Postoperative wound infection			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			



subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Sialoadenitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 1449 (0.28%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes ophthalmic			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Folate deficiency			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Anastrozole	Tamoxifen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1323 / 1449 (91.30%)	1380 / 1489 (92.68%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign breast neoplasm			
subjects affected / exposed	10 / 1449 (0.69%)	11 / 1489 (0.74%)	
occurrences (all)	10	11	
Breast cyst			
subjects affected / exposed	4 / 1449 (0.28%)	2 / 1489 (0.13%)	
occurrences (all)	4	2	
Fibroadenoma of breast			
subjects affected / exposed	6 / 1449 (0.41%)	8 / 1489 (0.54%)	
occurrences (all)	6	8	
Breast cancer in situ			
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)	
occurrences (all)	3	2	
Breast cancer metastatic			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences (all)	1	1	
Breast cancer recurrent			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Melanocytic naevus			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences (all)	1	1	
Skin papilloma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Adrenal adenoma			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Thyroid cyst		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Neuroendocrine carcinoma		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Anal polyp		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Colon adenoma		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gastric polyps		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Anal cancer		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Colon cancer		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Colorectal cancer stage IV		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gastrointestinal cancer metastatic		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gastrointestinal carcinoma		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Intestinal adenocarcinoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Lip and/or oral cavity cancer		

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Oesophageal carcinoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Rectal cancer		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Focal nodular hyperplasia		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Hepatic cancer		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Myelodysplastic syndrome		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Lymphoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Non-Hodgkin's lymphoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Mesothelioma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Metastases to bone		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Metastases to liver		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Metastases to lung		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Metastases to lymph nodes		

subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Metastases to peritoneum		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Metastases to skin		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Metastasis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Adenoma benign		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Cholesteatoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Cyst		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Polyp		
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)
occurrences (all)	0	3
Adenoid cystic carcinoma		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Angiosarcoma		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Carcinoma in situ		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Head and neck cancer		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Malignant neoplasm of unknown		

primary site		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Metastatic neoplasm		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Recurrent cancer		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Squamous cell carcinoma		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Neuroma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Intracranial meningioma malignant		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Meningioma		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gammopathy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Renal cancer		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Genital cyst		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cervical polyp		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Degeneration of uterine fibroid		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1

Ovarian cyst		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Uterine cyst		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Uterine leiomyoma		
subjects affected / exposed	0 / 1449 (0.00%)	6 / 1489 (0.40%)
occurrences (all)	0	6
Uterine polyp		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Vaginal polyp		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vulval polyp		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Endometrial cancer stage I		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Ovarian cancer		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Uterine cancer		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Vulval neoplasm		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Benign lung neoplasm		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Nasal polyps		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1



Adenosquamous cell lung cancer		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Bronchial carcinoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Lung adenocarcinoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Lung carcinoma cell type unspecified recurrent		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Lung carcinoma cell type unspecified stage 0		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Thymoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Tonsil cancer		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Basal cell carcinoma		
subjects affected / exposed	8 / 1449 (0.55%)	9 / 1489 (0.60%)
occurrences (all)	8	9
Bowen's disease		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Malignant melanoma		
subjects affected / exposed	4 / 1449 (0.28%)	1 / 1489 (0.07%)
occurrences (all)	4	1
Malignant melanoma in situ		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Melanoma recurrent		

subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Skin cancer			
subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	4 / 1489 (0.27%) 4	
Superficial spreading melanoma stage unspecified			
subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Lipoma			
subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	1 / 1489 (0.07%) 1	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Aneurysm			
subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Angina unstable			
subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Aortic stenosis			
subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Carotid artery occlusion			
subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Carotid artery stenosis			
subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Cerebrovascular accident			
subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Circulatory collapse			

subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Coronary artery disease		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Deep vein thrombosis		
subjects affected / exposed	5 / 1449 (0.35%)	3 / 1489 (0.20%)
occurrences (all)	5	3
Dizziness		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Embolism		
subjects affected / exposed	2 / 1449 (0.14%)	5 / 1489 (0.34%)
occurrences (all)	2	5
Epistaxis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Essential hypertension		
subjects affected / exposed	68 / 1449 (4.69%)	54 / 1489 (3.63%)
occurrences (all)	68	54
Femoral artery aneurysm		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Haematoma		
subjects affected / exposed	4 / 1449 (0.28%)	8 / 1489 (0.54%)
occurrences (all)	4	8
Haemorrhage intracranial		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Hot flush		
subjects affected / exposed	161 / 1449 (11.11%)	184 / 1489 (12.36%)
occurrences (all)	161	184
Hypertension		
subjects affected / exposed	28 / 1449 (1.93%)	22 / 1489 (1.48%)
occurrences (all)	28	22

Hypotension		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Ischaemia		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Ischaemic stroke		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Lymphoedema		
subjects affected / exposed	4 / 1449 (0.28%)	8 / 1489 (0.54%)
occurrences (all)	4	8
Malignant hypertension		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Orthostatic hypotension		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Peripheral coldness		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Peripheral vascular disorder		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Phlebitis		
subjects affected / exposed	3 / 1449 (0.21%)	7 / 1489 (0.47%)
occurrences (all)	3	7
Postmenopausal haemorrhage		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Presyncope		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Pulmonary embolism		
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)
occurrences (all)	3	2

Spider vein			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Temporal arteritis			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 1449 (0.07%)	6 / 1489 (0.40%)	
occurrences (all)	1	6	
Thrombosis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Transient ischaemic attack			
subjects affected / exposed	7 / 1449 (0.48%)	2 / 1489 (0.13%)	
occurrences (all)	7	2	
Varicose ulceration			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Varicose vein			
subjects affected / exposed	7 / 1449 (0.48%)	9 / 1489 (0.60%)	
occurrences (all)	7	9	
Vasculitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Venous insufficiency			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences (all)	3	0	
Venous thrombosis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Abscess drainage			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Acupuncture		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Adrenal gland operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Anal polypectomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Angioplasty		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Ankle operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Aortic valve replacement		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Appendicectomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Arterial stent insertion		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Arthroscopic surgery		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Bladder operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Bone lesion excision		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Bone operation		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Breast cyst drainage		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Breast lump removal		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Breast reconstruction		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Bunion operation		
subjects affected / exposed	6 / 1449 (0.41%)	8 / 1489 (0.54%)
occurrences (all)	6	8
Cancer surgery		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Cardiac ablation		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Cardiac operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cardiac pacemaker insertion		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cardiac resynchronisation therapy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cardioversion		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Carpal tunnel decompression		
subjects affected / exposed	13 / 1449 (0.90%)	3 / 1489 (0.20%)
occurrences (all)	13	3
Cataract operation		

subjects affected / exposed	18 / 1449 (1.24%)	26 / 1489 (1.75%)
occurrences (all)	18	26
Cervical polypectomy		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Chemotherapy		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Chiropractic		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cholecystectomy		
subjects affected / exposed	9 / 1449 (0.62%)	7 / 1489 (0.47%)
occurrences (all)	9	7
Colon operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Colon polypectomy		
subjects affected / exposed	3 / 1449 (0.21%)	6 / 1489 (0.40%)
occurrences (all)	3	6
Colonoscopy		
subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)
occurrences (all)	1	4
Colostomy		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Colporrhaphy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Coronary artery bypass		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Cyst removal		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Debridement		



subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dental care		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dental implantation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Dupuytren's contracture operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Ear operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Elbow operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Elective surgery		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Emergency care		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Endocervical curettage		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Ethmoid sinus surgery		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Eye operation		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Foot operation		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Gallbladder operation		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Haemorrhoid operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Hand repair operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Heart valve replacement		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Hernia repair		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
High frequency ablation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hip arthroplasty		
subjects affected / exposed	14 / 1449 (0.97%)	10 / 1489 (0.67%)
occurrences (all)	14	10
Hip surgery		
subjects affected / exposed	6 / 1449 (0.41%)	4 / 1489 (0.27%)
occurrences (all)	6	4
Hospitalisation		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Hysterectomy		
subjects affected / exposed	4 / 1449 (0.28%)	17 / 1489 (1.14%)
occurrences (all)	4	17
Ileostomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Incisional hernia repair		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Inguinal hernia repair		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Intervertebral disc operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Intestinal resection		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Intraocular lens implant		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Intra-uterine contraceptive device		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Jaw operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Joint manipulation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Joint surgery		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Knee arthroplasty		
subjects affected / exposed	12 / 1449 (0.83%)	13 / 1489 (0.87%)
occurrences (all)	12	13
Knee operation		
subjects affected / exposed	8 / 1449 (0.55%)	3 / 1489 (0.20%)
occurrences (all)	8	3
Large intestine operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Laryngeal polypectomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Lesion excision		

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Limb operation		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Lipoma excision		
subjects affected / exposed	0 / 1449 (0.00%)	7 / 1489 (0.47%)
occurrences (all)	0	7
Local anaesthesia		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Lung lobectomy		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Lymphadenectomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Mammoplasty		
subjects affected / exposed	3 / 1449 (0.21%)	4 / 1489 (0.27%)
occurrences (all)	3	4
Mastectomy		
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)
occurrences (all)	2	4
Meningioma surgery		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Meniscus removal		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Mitral valve replacement		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Mole excision		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Muscle operation		

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Nail operation		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Nasal operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Nephrectomy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Nerve block		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Oophorectomy		
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)
occurrences (all)	0	3
Oophorectomy bilateral		
subjects affected / exposed	2 / 1449 (0.14%)	5 / 1489 (0.34%)
occurrences (all)	2	5
Open reduction of fracture		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Ovarian cystectomy		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Parathyroidectomy		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Pelvic floor repair		
subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)
occurrences (all)	1	4
Physiotherapy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Plastic surgery		

subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Polypectomy		
subjects affected / exposed	1 / 1449 (0.07%)	12 / 1489 (0.81%)
occurrences (all)	1	12
Prolapse repair		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Prosthesis implantation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Radical mastectomy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Radiotherapy		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Renal cyst excision		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Retinal laser coagulation		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Retinal operation		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Salpingectomy		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Salpingo-oophorectomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Salpingo-oophorectomy bilateral		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Sclerotherapy		

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Shoulder arthroplasty		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Shoulder operation		
subjects affected / exposed	6 / 1449 (0.41%)	3 / 1489 (0.20%)
occurrences (all)	6	3
Simple mastectomy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Sinus operation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Skin graft		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Skin lesion excision		
subjects affected / exposed	5 / 1449 (0.35%)	3 / 1489 (0.20%)
occurrences (all)	5	3
Skin neoplasm excision		
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)
occurrences (all)	2	4
Spinal decompression		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Spinal laminectomy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Spinal operation		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Stent placement		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Steroid therapy		

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Surgery		
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)
occurrences (all)	4	4
Tendon operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Tendon sheath lesion excision		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Therapeutic skin care topical		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Thoracotomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Thyroid operation		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Thyroidectomy		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Toe amputation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Toe operation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Tooth extraction		
subjects affected / exposed	2 / 1449 (0.14%)	6 / 1489 (0.40%)
occurrences (all)	2	6
Trabeculectomy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Transfusion		



subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Tumour excision			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Umbilical hernia repair			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Uterine cervix dilation procedure			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Uterine cystectomy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Uterine dilation and curettage			
subjects affected / exposed	3 / 1449 (0.21%)	4 / 1489 (0.27%)	
occurrences (all)	3	4	
Uterine polypectomy			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences (all)	3	0	
Uterine prolapse repair			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Varicose vein operation			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Venous ligation			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Venous operation			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Vocal cordectomy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
General disorders and administration			

site conditions			
Pyrexia			
subjects affected / exposed	3 / 1449 (0.21%)	6 / 1489 (0.40%)	
occurrences (all)	3	6	
Asthenia			
subjects affected / exposed	23 / 1449 (1.59%)	25 / 1489 (1.68%)	
occurrences (all)	23	25	
Axillary pain			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Chest pain			
subjects affected / exposed	4 / 1449 (0.28%)	6 / 1489 (0.40%)	
occurrences (all)	4	6	
Chills			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Disease recurrence			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Facial pain			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Gait disturbance			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Hernia			
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)	
occurrences (all)	2	2	
Hot flush			

subjects affected / exposed	19 / 1449 (1.31%)	14 / 1489 (0.94%)
occurrences (all)	19	14
Inflammation		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Influenza like illness		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Irritability		
subjects affected / exposed	6 / 1449 (0.41%)	1 / 1489 (0.07%)
occurrences (all)	6	1
Lethargy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Malaise		
subjects affected / exposed	165 / 1449 (11.39%)	177 / 1489 (11.89%)
occurrences (all)	165	177
Night sweats		
subjects affected / exposed	5 / 1449 (0.35%)	3 / 1489 (0.20%)
occurrences (all)	5	3
Oedema		
subjects affected / exposed	21 / 1449 (1.45%)	28 / 1489 (1.88%)
occurrences (all)	21	28
Oedema peripheral		
subjects affected / exposed	18 / 1449 (1.24%)	9 / 1489 (0.60%)
occurrences (all)	18	9
Pain		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Polyp		
subjects affected / exposed	2 / 1449 (0.14%)	6 / 1489 (0.40%)
occurrences (all)	2	6
Thirst		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1

Adverse drug reaction subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Adverse reaction subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	0 / 1489 (0.00%) 0	
Cyst subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	2 / 1489 (0.13%) 2	
Dysplasia subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Fat necrosis subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	1 / 1489 (0.07%) 1	
Fibrosis subjects affected / exposed occurrences (all)	6 / 1449 (0.41%) 6	3 / 1489 (0.20%) 3	
Hyperplasia subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Immune system disorders			
Asthma subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	0 / 1489 (0.00%) 0	
Drug hypersensitivity subjects affected / exposed occurrences (all)	5 / 1449 (0.35%) 5	0 / 1489 (0.00%) 0	
Hypersensitivity subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	10 / 1489 (0.67%) 10	
Multiple allergies subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Antiphospholipid syndrome			

subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Polymyalgia rheumatica subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Rheumatoid arthritis subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Polyarteritis nodosa subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Temporal arteritis subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Social circumstances Bereavement subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Ex-tobacco user subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Reproductive system and breast disorders Adnexa uteri pain subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	3 / 1489 (0.20%) 3	
Arthritis climacteric subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Benign breast neoplasm subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Breast abscess subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Breast calcifications			

subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)
occurrences (all)	4	4
Breast cancer in situ		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Breast cancer metastatic		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Breast cancer recurrent		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Breast cyst		
subjects affected / exposed	10 / 1449 (0.69%)	7 / 1489 (0.47%)
occurrences (all)	10	7
Breast discharge		
subjects affected / exposed	6 / 1449 (0.41%)	5 / 1489 (0.34%)
occurrences (all)	6	5
Breast discomfort		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Breast disorder		
subjects affected / exposed	7 / 1449 (0.48%)	18 / 1489 (1.21%)
occurrences (all)	7	18
Breast hyperplasia		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Breast infection		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Breast necrosis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Breast pain		
subjects affected / exposed	70 / 1449 (4.83%)	66 / 1489 (4.43%)
occurrences (all)	70	66
Breast swelling		

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cervical dysplasia		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Cervical polyp		
subjects affected / exposed	2 / 1449 (0.14%)	11 / 1489 (0.74%)
occurrences (all)	2	11
Cystocele		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Dysmenorrhoea		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dyspareunia		
subjects affected / exposed	11 / 1449 (0.76%)	11 / 1489 (0.74%)
occurrences (all)	11	11
Endometrial disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Endometrial hyperplasia		
subjects affected / exposed	0 / 1449 (0.00%)	18 / 1489 (1.21%)
occurrences (all)	0	18
Endometrial hypertrophy		
subjects affected / exposed	2 / 1449 (0.14%)	34 / 1489 (2.28%)
occurrences (all)	2	34
Endometriosis		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Fibrocystic breast disease		
subjects affected / exposed	4 / 1449 (0.28%)	8 / 1489 (0.54%)
occurrences (all)	4	8
Galactorrhoea		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Gynaecomastia		

subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Hot flush		
subjects affected / exposed	815 / 1449 (56.25%)	898 / 1489 (60.31%)
occurrences (all)	815	898
Intraductal papilloma of breast		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Mastitis		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Menopausal symptoms		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Menorrhagia		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Metrorrhagia		
subjects affected / exposed	13 / 1449 (0.90%)	20 / 1489 (1.34%)
occurrences (all)	13	20
Night sweats		
subjects affected / exposed	70 / 1449 (4.83%)	74 / 1489 (4.97%)
occurrences (all)	70	74
Nipple disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Nipple pain		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Ovarian cyst		
subjects affected / exposed	10 / 1449 (0.69%)	9 / 1489 (0.60%)
occurrences (all)	10	9
Ovarian mass		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1



Pelvic pain		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Perineal pain		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Postmenopausal haemorrhage		
subjects affected / exposed	13 / 1449 (0.90%)	12 / 1489 (0.81%)
occurrences (all)	13	12
Premenstrual syndrome		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Sexual dysfunction		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Uterine atrophy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Uterine cyst		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Uterine fibrosis		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Uterine haemorrhage		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Uterine leiomyoma		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Uterine polyp		
subjects affected / exposed	9 / 1449 (0.62%)	25 / 1489 (1.68%)
occurrences (all)	9	25
Uterine prolapse		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1

Uterine spasm		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Vaginal cyst		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Vaginal discharge		
subjects affected / exposed	31 / 1449 (2.14%)	140 / 1489 (9.40%)
occurrences (all)	31	140
Vaginal disorder		
subjects affected / exposed	20 / 1449 (1.38%)	22 / 1489 (1.48%)
occurrences (all)	20	22
Vaginal haemorrhage		
subjects affected / exposed	32 / 1449 (2.21%)	78 / 1489 (5.24%)
occurrences (all)	32	78
Vaginal inflammation		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Vaginal polyp		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Vaginal prolapse		
subjects affected / exposed	8 / 1449 (0.55%)	11 / 1489 (0.74%)
occurrences (all)	8	11
Vaginal swelling		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vulval abscess		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vulval neoplasm		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Vulval polyp		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1

Vulvovaginal dryness subjects affected / exposed occurrences (all)	201 / 1449 (13.87%) 201	166 / 1489 (11.15%) 166	
Vulvovaginal pain subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	19 / 1449 (1.31%) 19	47 / 1489 (3.16%) 47	
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	10 / 1449 (0.69%) 10	12 / 1489 (0.81%) 12	
Bronchitis chronic subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	2 / 1489 (0.13%) 2	
Chest discomfort subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Chest pain subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	4 / 1449 (0.28%) 4	6 / 1489 (0.40%) 6	
Cough subjects affected / exposed occurrences (all)	16 / 1449 (1.10%) 16	24 / 1489 (1.61%) 24	
Dry throat subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	21 / 1449 (1.45%) 21	30 / 1489 (2.01%) 30	
Dyspnoea exertional			

subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Emphysema		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Epistaxis		
subjects affected / exposed	5 / 1449 (0.35%)	3 / 1489 (0.20%)
occurrences (all)	5	3
Haemoptysis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Increased upper airway secretion		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Lobar pneumonia		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Lower respiratory tract infection		
subjects affected / exposed	22 / 1449 (1.52%)	53 / 1489 (3.56%)
occurrences (all)	22	53
Lung cancer metastatic		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Lung disorder		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Multifocal micronodular pneumocyte hyperplasia		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Nasal congestion		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Nasal discomfort		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2

Nasal dryness		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Nasal polyps		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Pertussis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Pleurisy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Pleuritic pain		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Pneumonia		
subjects affected / exposed	7 / 1449 (0.48%)	3 / 1489 (0.20%)
occurrences (all)	7	3
Pulmonary arterial hypertension		
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)
occurrences (all)	4	4
Pulmonary embolism		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Pulmonary hypertension		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Respiratory disorder		
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)
occurrences (all)	2	4
Respiratory distress		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Rhinitis allergic		
subjects affected / exposed	2 / 1449 (0.14%)	5 / 1489 (0.34%)
occurrences (all)	2	5

Rhinorrhoea			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Sleep apnoea syndrome			
subjects affected / exposed	24 / 1449 (1.66%)	25 / 1489 (1.68%)	
occurrences (all)	24	25	
Throat tightness			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Tonsillar disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	4 / 1449 (0.28%)	7 / 1489 (0.47%)	
occurrences (all)	4	7	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Amnesia			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Aggression			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Alcohol problem			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Anxiety			

subjects affected / exposed	15 / 1449 (1.04%)	22 / 1489 (1.48%)
occurrences (all)	15	22
Bipolar I disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Cognitive disorder		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Depression		
subjects affected / exposed	67 / 1449 (4.62%)	70 / 1489 (4.70%)
occurrences (all)	67	70
Eating disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Emotional disorder		
subjects affected / exposed	27 / 1449 (1.86%)	36 / 1489 (2.42%)
occurrences (all)	27	36
Hallucination		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Insomnia		
subjects affected / exposed	109 / 1449 (7.52%)	93 / 1489 (6.25%)
occurrences (all)	109	93
Loss of libido		
subjects affected / exposed	10 / 1449 (0.69%)	12 / 1489 (0.81%)
occurrences (all)	10	12
Mental disorder		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Nervousness		
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)
occurrences (all)	3	2
Neurosis		
subjects affected / exposed	0 / 1449 (0.00%)	5 / 1489 (0.34%)
occurrences (all)	0	5
Nightmare		

subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Personality disorder			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences (all)	3	0	
Phobia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences (all)	2	3	
Sleep disorder			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Stress			
subjects affected / exposed	4 / 1449 (0.28%)	5 / 1489 (0.34%)	
occurrences (all)	4	5	
Suicidal ideation			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Cholecystitis acute			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Cholecystitis chronic			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Cholelithiasis			
subjects affected / exposed	4 / 1449 (0.28%)	8 / 1489 (0.54%)	
occurrences (all)	4	8	



Gallbladder disorder subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Haemochromatosis subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	2 / 1489 (0.13%) 2	
Hepatic cirrhosis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Hepatitis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	3 / 1489 (0.20%) 3	
Liver disorder subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	3 / 1489 (0.20%) 3	
Hepatobiliary carcinoma in situ subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Investigations			
Biopsy lymph gland subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Angiogram subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Arteriogram coronary subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Blood pressure subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	2 / 1489 (0.13%) 2	
Blood pressure abnormal subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Blood pressure increased			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cardiac murmur		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cardiovascular evaluation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Catheterisation cardiac		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Echocardiogram		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Electrocardiogram		
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)
occurrences (all)	3	2
Electrocardiogram abnormal		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Electrocardiogram ST segment depression		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Heart rate decreased		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Heart rate irregular		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Scan myocardial perfusion		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Ultrasound Doppler		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2

Venogram		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Gene mutation identification test positive		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Biopsy thyroid gland		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Thyroid function test abnormal		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Barium enema		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Barium swallow		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Biopsy colon abnormal		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Biopsy oesophagus		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Colonoscopy		
subjects affected / exposed	0 / 1449 (0.00%)	5 / 1489 (0.34%)
occurrences (all)	0	5
Endoscopy upper gastrointestinal tract		
subjects affected / exposed	2 / 1449 (0.14%)	5 / 1489 (0.34%)
occurrences (all)	2	5
Oesophagogastrectomy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Sigmoidoscopy		

subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Ultrasound abdomen		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
White blood cell count decreased		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Red blood cell count		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Biopsy liver		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Hepatic enzyme increased		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Liver function test abnormal		
subjects affected / exposed	17 / 1449 (1.17%)	21 / 1489 (1.41%)
occurrences (all)	17	21
Ultrasound biliary tract		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Biopsy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Computerised tomogram		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Endoscopy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0

Imaging procedure		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Investigation		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Needle biopsy site unspecified normal		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Nuclear magnetic resonance imaging		
subjects affected / exposed	4 / 1449 (0.28%)	2 / 1489 (0.13%)
occurrences (all)	4	2
X-ray		
subjects affected / exposed	4 / 1449 (0.28%)	2 / 1489 (0.13%)
occurrences (all)	4	2
Free fatty acids increased		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Glucose tolerance test		
subjects affected / exposed	5 / 1449 (0.35%)	3 / 1489 (0.20%)
occurrences (all)	5	3
Arthroscopy		
subjects affected / exposed	6 / 1449 (0.41%)	7 / 1489 (0.47%)
occurrences (all)	6	7
Bone densitometry		
subjects affected / exposed	4 / 1449 (0.28%)	3 / 1489 (0.20%)
occurrences (all)	4	3
Bone density decreased		
subjects affected / exposed	56 / 1449 (3.86%)	42 / 1489 (2.82%)
occurrences (all)	56	42
Acoustic stimulation tests		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Brain scan normal		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Scan brain		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Body height decreased		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Body temperature increased		
subjects affected / exposed	4 / 1449 (0.28%)	1 / 1489 (0.07%)
occurrences (all)	4	1
Gastrointestinal examination		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Gynaecological examination		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Neurological examination		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Ophthalmological examination		
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)
occurrences (all)	4	4
Orthopaedic examination		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Weight decreased		
subjects affected / exposed	23 / 1449 (1.59%)	15 / 1489 (1.01%)
occurrences (all)	23	15
Weight increased		
subjects affected / exposed	126 / 1449 (8.70%)	133 / 1489 (8.93%)
occurrences (all)	126	133
Cystoscopy		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Ultrasound kidney		

subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Aspiration breast		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Biopsy breast		
subjects affected / exposed	8 / 1449 (0.55%)	12 / 1489 (0.81%)
occurrences (all)	8	12
Biopsy breast normal		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Biopsy cervix		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Biopsy endometrium		
subjects affected / exposed	2 / 1449 (0.14%)	7 / 1489 (0.47%)
occurrences (all)	2	7
Biopsy endometrium normal		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Biopsy testes normal		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Biopsy uterus		
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)
occurrences (all)	0	3
Biopsy vagina		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Hysteroscopy		
subjects affected / exposed	4 / 1449 (0.28%)	16 / 1489 (1.07%)
occurrences (all)	4	16
Mammogram		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Mammogram abnormal		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Mammogram normal		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Smear cervix		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Smear cervix abnormal		
subjects affected / exposed	1 / 1449 (0.07%)	6 / 1489 (0.40%)
occurrences (all)	1	6
Ultrasound breast		
subjects affected / exposed	2 / 1449 (0.14%)	10 / 1489 (0.67%)
occurrences (all)	2	10
Ultrasound pelvis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Ultrasound scan vagina		
subjects affected / exposed	0 / 1449 (0.00%)	4 / 1489 (0.27%)
occurrences (all)	0	4
Ultrasound uterus		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Chest X-ray		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Computerised tomogram thorax		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Laryngoscopy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Sclerotherapy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Serum ferritin increased		



subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	9 / 1449 (0.62%)	10 / 1489 (0.67%)	
occurrences (all)	9	10	
Bone fragmentation			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Bursa injury			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Cartilage injury			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences (all)	1	1	
Cervical vertebral fracture			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Clavicle fracture			
subjects affected / exposed	0 / 1449 (0.00%)	4 / 1489 (0.27%)	
occurrences (all)	0	4	
Facial bones fracture			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Femoral neck fracture			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Femur fracture			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Fibula fracture			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Foot fracture			

subjects affected / exposed	14 / 1449 (0.97%)	17 / 1489 (1.14%)
occurrences (all)	14	17
Forearm fracture		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Fracture		
subjects affected / exposed	5 / 1449 (0.35%)	5 / 1489 (0.34%)
occurrences (all)	5	5
Fracture displacement		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Fractured coccyx		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Fractured sacrum		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Haemarthrosis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hand fracture		
subjects affected / exposed	7 / 1449 (0.48%)	7 / 1489 (0.47%)
occurrences (all)	7	7
Hip fracture		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Humerus fracture		
subjects affected / exposed	6 / 1449 (0.41%)	1 / 1489 (0.07%)
occurrences (all)	6	1
Joint dislocation		
subjects affected / exposed	5 / 1449 (0.35%)	6 / 1489 (0.40%)
occurrences (all)	5	6
Lower limb fracture		
subjects affected / exposed	3 / 1449 (0.21%)	4 / 1489 (0.27%)
occurrences (all)	3	4
Meniscus injury		

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Meniscus lesion		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Multiple fractures		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Patella fracture		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Pelvic fracture		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Radius fracture		
subjects affected / exposed	6 / 1449 (0.41%)	2 / 1489 (0.13%)
occurrences (all)	6	2
Rib fracture		
subjects affected / exposed	7 / 1449 (0.48%)	6 / 1489 (0.40%)
occurrences (all)	7	6
Skull fracture		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Spinal fracture		
subjects affected / exposed	5 / 1449 (0.35%)	7 / 1489 (0.47%)
occurrences (all)	5	7
Traumatic fracture		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Ulna fracture		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Upper limb fracture		
subjects affected / exposed	18 / 1449 (1.24%)	7 / 1489 (0.47%)
occurrences (all)	18	7
Wrist fracture		

subjects affected / exposed	30 / 1449 (2.07%)	15 / 1489 (1.01%)
occurrences (all)	30	15
Food poisoning		
subjects affected / exposed	6 / 1449 (0.41%)	7 / 1489 (0.47%)
occurrences (all)	6	7
Animal bite		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Corneal abrasion		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Excoriation		
subjects affected / exposed	10 / 1449 (0.69%)	9 / 1489 (0.60%)
occurrences (all)	10	9
Fall		
subjects affected / exposed	19 / 1449 (1.31%)	16 / 1489 (1.07%)
occurrences (all)	19	16
Injury		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Ligament injury		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Ligament rupture		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Mouth injury		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Muscle rupture		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Perineal laceration		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Retinal detachment		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Road traffic accident		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Soft tissue injury		
subjects affected / exposed	10 / 1449 (0.69%)	13 / 1489 (0.87%)
occurrences (all)	10	13
Superficial injury of eye		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Tendon rupture		
subjects affected / exposed	4 / 1449 (0.28%)	1 / 1489 (0.07%)
occurrences (all)	4	1
Tooth injury		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Vascular injury		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Vena cava injury		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vitreous detachment		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Deep vein thrombosis postoperative		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Device intolerance		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Implant tissue necrosis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Post procedural complication		

subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Post procedural haemorrhage subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Postoperative thrombosis subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Postoperative wound complication subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Procedural pain subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	11 / 1489 (0.74%) 11	
Seroma subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Vascular graft occlusion subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Congenital, familial and genetic disorders			
Gastrointestinal angiodysplasia subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Heart disease congenital subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Cataract congenital subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Haemangioma of retina subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Osteoporosis			

subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Congenital cystic kidney disease subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	0 / 1489 (0.00%) 0	
Basal cell naevus syndrome subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Keratosis follicular subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Cardiac disorders			
Arrhythmia subjects affected / exposed occurrences (all)	5 / 1449 (0.35%) 5	7 / 1489 (0.47%) 7	
Atrial fibrillation subjects affected / exposed occurrences (all)	5 / 1449 (0.35%) 5	7 / 1489 (0.47%) 7	
Atrial flutter subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Atrial tachycardia subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Bradyarrhythmia subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Tachycardia subjects affected / exposed occurrences (all)	9 / 1449 (0.62%) 9	9 / 1489 (0.60%) 9	
Cardiac discomfort subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Cardiac disorder subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	1 / 1489 (0.07%) 1	

Cardiovascular disorder		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Dizziness		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dyspnoea		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Palpitations		
subjects affected / exposed	19 / 1449 (1.31%)	18 / 1489 (1.21%)
occurrences (all)	19	18
Aortic valve incompetence		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Aortic valve stenosis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Mitral valve incompetence		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Mitral valve prolapse		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Angina pectoris		
subjects affected / exposed	6 / 1449 (0.41%)	0 / 1489 (0.00%)
occurrences (all)	6	0
Angina unstable		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Chest pain		
subjects affected / exposed	14 / 1449 (0.97%)	15 / 1489 (1.01%)
occurrences (all)	14	15
Coronary artery disease		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0



Coronary artery stenosis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Myocardial infarction		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Myocardial ischaemia		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Endocarditis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cardiac failure		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cardiac failure chronic		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Left ventricular failure		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Cardiomegaly		
subjects affected / exposed	2 / 1449 (0.14%)	6 / 1489 (0.40%)
occurrences (all)	2	6
Cardiomyopathy		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Ventricular dysfunction		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Dressler's syndrome		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Pericardial effusion		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1

Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Cerebral vasoconstriction			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Cerebrovascular accident			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences (all)	2	1	
Haemorrhagic stroke			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Ischaemic stroke			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Temporal arteritis			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Transient ischaemic attack			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences (all)	3	1	
Anosmia			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Cranial nerve paralysis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Facial palsy			
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)	
occurrences (all)	1	3	
Facial spasm			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Neuritis cranial			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Optic neuritis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vith nerve paralysis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Multiple sclerosis		
subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)
occurrences (all)	1	4
Headache		
subjects affected / exposed	82 / 1449 (5.66%)	61 / 1489 (4.10%)
occurrences (all)	82	61
Migraine		
subjects affected / exposed	10 / 1449 (0.69%)	10 / 1489 (0.67%)
occurrences (all)	10	10
Migraine with aura		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Tension headache		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Amnesia		
subjects affected / exposed	27 / 1449 (1.86%)	28 / 1489 (1.88%)
occurrences (all)	27	28
Cognitive disorder		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Dementia Alzheimer's type		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dementia of the Alzheimer's type, with depressed mood		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0

Disturbance in attention subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	4 / 1489 (0.27%) 4
Memory impairment subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1
Essential tremor subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Parkinsonism subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0
Parkinson's disease subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	1 / 1489 (0.07%) 1
Spastic paralysis subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Torticollis subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Tremor subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	10 / 1489 (0.67%) 10
Ageusia subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Analgesia subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Aphonia subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	6 / 1489 (0.40%) 6
Balance disorder subjects affected / exposed occurrences (all)	35 / 1449 (2.42%) 35	35 / 1489 (2.35%) 35

Confusional state		
subjects affected / exposed	4 / 1449 (0.28%)	2 / 1489 (0.13%)
occurrences (all)	4	2
Coordination abnormal		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dizziness		
subjects affected / exposed	7 / 1449 (0.48%)	8 / 1489 (0.54%)
occurrences (all)	7	8
Dizziness postural		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dysaesthesia		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dysgeusia		
subjects affected / exposed	11 / 1449 (0.76%)	3 / 1489 (0.20%)
occurrences (all)	11	3
Hypoaesthesia		
subjects affected / exposed	10 / 1449 (0.69%)	10 / 1489 (0.67%)
occurrences (all)	10	10
Lethargy		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Loss of consciousness		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Neuralgia		
subjects affected / exposed	5 / 1449 (0.35%)	4 / 1489 (0.27%)
occurrences (all)	5	4
Neurological symptom		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Paraesthesia		
subjects affected / exposed	43 / 1449 (2.97%)	23 / 1489 (1.54%)
occurrences (all)	43	23

Presyncope		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Restless legs syndrome		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Sensory disturbance		
subjects affected / exposed	8 / 1449 (0.55%)	1 / 1489 (0.07%)
occurrences (all)	8	1
Somnolence		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Syncope		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vertigo		
subjects affected / exposed	15 / 1449 (1.04%)	17 / 1489 (1.14%)
occurrences (all)	15	17
Muscle rigidity		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Carpal tunnel syndrome		
subjects affected / exposed	35 / 1449 (2.42%)	13 / 1489 (0.87%)
occurrences (all)	35	13
Guillain-Barre syndrome		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Nerve compression		
subjects affected / exposed	4 / 1449 (0.28%)	2 / 1489 (0.13%)
occurrences (all)	4	2
Neuropathy peripheral		
subjects affected / exposed	17 / 1449 (1.17%)	14 / 1489 (0.94%)
occurrences (all)	17	14
Convulsion		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1

Epilepsy			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences (all)	3	0	
Insomnia			
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)	
occurrences (all)	3	0	
Narcolepsy			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences (all)	0	3	
Radiculopathy			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	10 / 1449 (0.69%)	11 / 1489 (0.74%)	
occurrences (all)	10	11	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)	
occurrences (all)	3	3	
Anaemia macrocytic			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Coagulopathy			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Increased tendency to bruise			
subjects affected / exposed	0 / 1449 (0.00%)	4 / 1489 (0.27%)	
occurrences (all)	0	4	
Blood disorder			
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)	
occurrences (all)	3	2	
Haemolytic anaemia			

subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Gammopathy			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Multiple myeloma			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Lymphadenopathy			
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Lymphoedema			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)	
occurrences (all)	4	4	
Neutropenia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Cholesteatoma			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	



Ear pain			
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences (all)	2	3	
Deafness			
subjects affected / exposed	6 / 1449 (0.41%)	5 / 1489 (0.34%)	
occurrences (all)	6	5	
Hearing impaired			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Meniere's disease			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	7 / 1449 (0.48%)	4 / 1489 (0.27%)	
occurrences (all)	7	4	
Vertigo			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences (all)	3	1	
Mastoid disorder			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Mastoiditis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Middle ear adhesions			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Tympanic membrane perforation			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences (all)	1	1	
Eye disorders			
Cataract			
subjects affected / exposed	77 / 1449 (5.31%)	64 / 1489 (4.30%)	
occurrences (all)	77	64	
Cataract congenital			

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Cataract diabetic		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cataract nuclear		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Entropion		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Corneal disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Dry eye		
subjects affected / exposed	35 / 1449 (2.42%)	49 / 1489 (3.29%)
occurrences (all)	35	49
Eye disorder		
subjects affected / exposed	38 / 1449 (2.62%)	35 / 1489 (2.35%)
occurrences (all)	38	35
Eye pain		
subjects affected / exposed	8 / 1449 (0.55%)	5 / 1489 (0.34%)
occurrences (all)	8	5
Eyelid disorder		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Lacrimation increased		
subjects affected / exposed	12 / 1449 (0.83%)	7 / 1489 (0.47%)
occurrences (all)	12	7
Vitreous disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Borderline glaucoma		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Glaucoma		

subjects affected / exposed	21 / 1449 (1.45%)	15 / 1489 (1.01%)
occurrences (all)	21	15
Ocular hypertension		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Conjunctival haemorrhage		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Eye haemorrhage		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Blepharitis		
subjects affected / exposed	7 / 1449 (0.48%)	3 / 1489 (0.20%)
occurrences (all)	7	3
Conjunctivitis		
subjects affected / exposed	5 / 1449 (0.35%)	6 / 1489 (0.40%)
occurrences (all)	5	6
Episcleritis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Eye irritation		
subjects affected / exposed	9 / 1449 (0.62%)	8 / 1489 (0.54%)
occurrences (all)	9	8
Ocular hyperaemia		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Haemangioma of retina		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Blepharospasm		
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)
occurrences (all)	0	3
Macular degeneration		
subjects affected / exposed	8 / 1449 (0.55%)	5 / 1489 (0.34%)
occurrences (all)	8	5
Macular hole		

subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Retinal detachment		
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)
occurrences (all)	4	4
Retinal tear		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vitreous detachment		
subjects affected / exposed	6 / 1449 (0.41%)	4 / 1489 (0.27%)
occurrences (all)	6	4
Diabetic retinopathy		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Retinal artery occlusion		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Retinal vein occlusion		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Retinal vein thrombosis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Blindness		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Diplopia		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Myopia		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Vision blurred		
subjects affected / exposed	12 / 1449 (0.83%)	18 / 1489 (1.21%)
occurrences (all)	12	18
Visual acuity reduced		

subjects affected / exposed	40 / 1449 (2.76%)	42 / 1489 (2.82%)	
occurrences (all)	40	42	
Visual impairment			
subjects affected / exposed	11 / 1449 (0.76%)	14 / 1489 (0.94%)	
occurrences (all)	11	14	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 1449 (0.00%)	4 / 1489 (0.27%)	
occurrences (all)	0	4	
Femoral hernia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Hiatus hernia			
subjects affected / exposed	6 / 1449 (0.41%)	5 / 1489 (0.34%)	
occurrences (all)	6	5	
Inguinal hernia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Lumbar hernia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Anal fissure			
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)	
occurrences (all)	2	3	
Anal pruritus			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Anorectal disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Anorectal squamous cell metaplasia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Rectal prolapse			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences (all)	3	1	

Anal polyp		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Colonic polyp		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Gastric polyps		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Intestinal polyp		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Rectal polyp		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Gingival disorder		
subjects affected / exposed	8 / 1449 (0.55%)	5 / 1489 (0.34%)
occurrences (all)	8	5
Gingivitis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Poor dental condition		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Tooth fracture		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Toothache		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Diverticulitis		
subjects affected / exposed	7 / 1449 (0.48%)	9 / 1489 (0.60%)
occurrences (all)	7	9
Diverticulitis intestinal haemorrhagic		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1

Diverticulum		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Barrett's oesophagus		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Food poisoning		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gastric disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Gastric mucosal hypertrophy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gastrointestinal disorder		
subjects affected / exposed	4 / 1449 (0.28%)	12 / 1489 (0.81%)
occurrences (all)	4	12
Oesophageal disorder		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Haematemesis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Haematochezia		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Rectal haemorrhage		
subjects affected / exposed	2 / 1449 (0.14%)	9 / 1489 (0.60%)
occurrences (all)	2	9
Small intestinal haemorrhage		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Colitis		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3

Colitis ischaemic		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Colitis ulcerative		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gastritis		
subjects affected / exposed	12 / 1449 (0.83%)	13 / 1489 (0.87%)
occurrences (all)	12	13
Gastrointestinal inflammation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Inflammatory bowel disease		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Oesophagitis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Proctocolitis		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Reflux oesophagitis		
subjects affected / exposed	17 / 1449 (1.17%)	18 / 1489 (1.21%)
occurrences (all)	17	18
Change of bowel habit		
subjects affected / exposed	5 / 1449 (0.35%)	2 / 1489 (0.13%)
occurrences (all)	5	2
Constipation		
subjects affected / exposed	24 / 1449 (1.66%)	42 / 1489 (2.82%)
occurrences (all)	24	42
Diarrhoea		
subjects affected / exposed	20 / 1449 (1.38%)	18 / 1489 (1.21%)
occurrences (all)	20	18
Duodenogastric reflux		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1



Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	2 / 1489 (0.13%) 2
Irritable bowel syndrome subjects affected / exposed occurrences (all)	5 / 1449 (0.35%) 5	3 / 1489 (0.20%) 3
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Abdominal distension subjects affected / exposed occurrences (all)	15 / 1449 (1.04%) 15	11 / 1489 (0.74%) 11
Abdominal mass subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	2 / 1489 (0.13%) 2
Abdominal pain subjects affected / exposed occurrences (all)	33 / 1449 (2.28%) 33	48 / 1489 (3.22%) 48
Dyspepsia subjects affected / exposed occurrences (all)	25 / 1449 (1.73%) 25	24 / 1489 (1.61%) 24
Dysphagia subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	1 / 1489 (0.07%) 1
Epigastric discomfort subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Flatulence subjects affected / exposed occurrences (all)	9 / 1449 (0.62%) 9	10 / 1489 (0.67%) 10
Gastrointestinal pain subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Nausea subjects affected / exposed occurrences (all)	57 / 1449 (3.93%) 57	51 / 1489 (3.43%) 51

Pelvic pain		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vomiting		
subjects affected / exposed	9 / 1449 (0.62%)	7 / 1489 (0.47%)
occurrences (all)	9	7
Gallstone ileus		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Intestinal obstruction		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Gastric ulcer		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Large intestine perforation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Haemorrhoids		
subjects affected / exposed	6 / 1449 (0.41%)	7 / 1489 (0.47%)
occurrences (all)	6	7
Coeliac disease		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Anal cancer		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Rectal cancer		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Mouth ulceration		
subjects affected / exposed	3 / 1449 (0.21%)	7 / 1489 (0.47%)
occurrences (all)	3	7
Oral pain		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1

Stomatitis			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Abdominal adhesions			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	25 / 1449 (1.73%)	16 / 1489 (1.07%)	
occurrences (all)	25	16	
Dry throat			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Lip dry			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Salivary gland cyst			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Salivary gland disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Ageusia			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Glossitis			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Tongue disorder			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 1449 (0.00%)	4 / 1489 (0.27%)	
occurrences (all)	0	4	
Actinic keratosis			

subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Alopecia		
subjects affected / exposed	80 / 1449 (5.52%)	93 / 1489 (6.25%)
occurrences (all)	80	93
Alopecia areata		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Basal cell carcinoma		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Basal cell naevus syndrome		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Blister		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Bowen's disease		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Cellulitis		
subjects affected / exposed	2 / 1449 (0.14%)	4 / 1489 (0.27%)
occurrences (all)	2	4
Dermal cyst		
subjects affected / exposed	6 / 1449 (0.41%)	5 / 1489 (0.34%)
occurrences (all)	6	5
Dermatomyositis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Dry skin		
subjects affected / exposed	27 / 1449 (1.86%)	28 / 1489 (1.88%)
occurrences (all)	27	28
Eczema		
subjects affected / exposed	6 / 1449 (0.41%)	18 / 1489 (1.21%)
occurrences (all)	6	18
Erythema		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Erythema multiforme		
subjects affected / exposed	5 / 1449 (0.35%)	3 / 1489 (0.20%)
occurrences (all)	5	3
Erythema nodosum		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hair colour changes		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hair disorder		
subjects affected / exposed	5 / 1449 (0.35%)	11 / 1489 (0.74%)
occurrences (all)	5	11
Hirsutism		
subjects affected / exposed	6 / 1449 (0.41%)	12 / 1489 (0.81%)
occurrences (all)	6	12
Hyperhidrosis		
subjects affected / exposed	25 / 1449 (1.73%)	18 / 1489 (1.21%)
occurrences (all)	25	18
Lichen planus		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Lichen sclerosis		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Morphoea		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Nail disorder		
subjects affected / exposed	6 / 1449 (0.41%)	13 / 1489 (0.87%)
occurrences (all)	6	13
Night sweats		
subjects affected / exposed	310 / 1449 (21.39%)	341 / 1489 (22.90%)
occurrences (all)	310	341

Onychoclasia		
subjects affected / exposed	6 / 1449 (0.41%)	16 / 1489 (1.07%)
occurrences (all)	6	16
Periorbital oedema		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Photosensitivity reaction		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Pigmentation disorder		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Pruritus		
subjects affected / exposed	22 / 1449 (1.52%)	38 / 1489 (2.55%)
occurrences (all)	22	38
Pruritus generalised		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Psoriasis		
subjects affected / exposed	6 / 1449 (0.41%)	3 / 1489 (0.20%)
occurrences (all)	6	3
Rash		
subjects affected / exposed	26 / 1449 (1.79%)	37 / 1489 (2.48%)
occurrences (all)	26	37
Rash erythematous		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Rash pruritic		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Rash scarlatiniform		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Rosacea		
subjects affected / exposed	1 / 1449 (0.07%)	6 / 1489 (0.40%)
occurrences (all)	1	6

Scar		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Scar pain		
subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)
occurrences (all)	1	4
Skin atrophy		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Skin cancer		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Skin disorder		
subjects affected / exposed	12 / 1449 (0.83%)	12 / 1489 (0.81%)
occurrences (all)	12	12
Skin lesion		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Skin mass		
subjects affected / exposed	3 / 1449 (0.21%)	2 / 1489 (0.13%)
occurrences (all)	3	2
Skin swelling		
subjects affected / exposed	2 / 1449 (0.14%)	6 / 1489 (0.40%)
occurrences (all)	2	6
Skin ulcer		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Skin warm		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Superficial spreading melanoma stage unspecified		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Swelling face		

subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)	
occurrences (all)	1	2	
Telangiectasia			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences (all)	0	3	
Urticaria			
subjects affected / exposed	6 / 1449 (0.41%)	11 / 1489 (0.74%)	
occurrences (all)	6	11	
Varicella			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Vitiligo			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Bladder disorder			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Bladder prolapse			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Calculus bladder			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Chromaturia			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences (all)	1	1	
Dysuria			
subjects affected / exposed	2 / 1449 (0.14%)	6 / 1489 (0.40%)	
occurrences (all)	2	6	
Haematuria			
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)	
occurrences (all)	2	1	



Haemorrhage urinary tract subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0
Micturition disorder subjects affected / exposed occurrences (all)	7 / 1449 (0.48%) 7	16 / 1489 (1.07%) 16
Micturition urgency subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	0 / 1489 (0.00%) 0
Nephrolithiasis subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	0 / 1489 (0.00%) 0
Nocturia subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1
Pollakiuria subjects affected / exposed occurrences (all)	6 / 1449 (0.41%) 6	10 / 1489 (0.67%) 10
Polyuria subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1
Renal colic subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	2 / 1489 (0.13%) 2
Renal cyst subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0
Renal disorder subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0
Renal failure chronic subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0
Renal tubular acidosis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0

Stress urinary incontinence subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	3 / 1489 (0.20%) 3	
Urethral stenosis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Urinary incontinence subjects affected / exposed occurrences (all)	6 / 1449 (0.41%) 6	15 / 1489 (1.01%) 15	
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Endocrine disorders			
Adrenal adenoma subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Adrenal carcinoma subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Adrenal disorder subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Adrenal mass subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Diabetes mellitus subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	0 / 1489 (0.00%) 0	
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	4 / 1489 (0.27%) 4	
Hypoparathyroidism subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Parathyroid disorder			

subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Goitre subjects affected / exposed occurrences (all)	6 / 1449 (0.41%) 6	5 / 1489 (0.34%) 5	
Hyperthyroidism subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	0 / 1489 (0.00%) 0	
Hypothyroidism subjects affected / exposed occurrences (all)	12 / 1449 (0.83%) 12	16 / 1489 (1.07%) 16	
Thyroid cyst subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	2 / 1489 (0.13%) 2	
Thyroid disorder subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	2 / 1489 (0.13%) 2	
Musculoskeletal and connective tissue disorders			
Bone erosion subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Exostosis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Jaw disorder subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Osteitis deformans subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	2 / 1489 (0.13%) 2	
Osteonecrosis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Osteopenia			

subjects affected / exposed	11 / 1449 (0.76%)	4 / 1489 (0.27%)
occurrences (all)	11	4
Osteoporosis		
subjects affected / exposed	106 / 1449 (7.32%)	71 / 1489 (4.77%)
occurrences (all)	106	71
Osteoporosis postmenopausal		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Pain in jaw		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Spinal disorder		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
CREST syndrome		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Morphoea		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Polymyalgia rheumatica		
subjects affected / exposed	5 / 1449 (0.35%)	2 / 1489 (0.13%)
occurrences (all)	5	2
Scleroderma		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Sjogren's syndrome		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Ankle fracture		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Clavicle fracture		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Fibula fracture		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Foot fracture		
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)
occurrences (all)	2	2
Forearm fracture		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Fractured coccyx		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hand fracture		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Hip fracture		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Humerus fracture		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Lower limb fracture		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Osteoporotic fracture		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Pathological fracture		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Radius fracture		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Rib fracture		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Spinal fracture		

subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)	
occurrences (all)	2	2	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Upper limb fracture			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Wrist fracture			
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)	
occurrences (all)	3	1	
Ankylosing spondylitis			
subjects affected / exposed	2 / 1449 (0.14%)	2 / 1489 (0.13%)	
occurrences (all)	2	2	
Arthralgia			
subjects affected / exposed	842 / 1449 (58.11%)	748 / 1489 (50.24%)	
occurrences (all)	842	748	
Arthritis			
subjects affected / exposed	52 / 1449 (3.59%)	50 / 1489 (3.36%)	
occurrences (all)	52	50	
Arthritis bacterial			
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)	
occurrences (all)	1	1	
Arthritis infective			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Arthritis reactive			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Arthropathy			
subjects affected / exposed	11 / 1449 (0.76%)	9 / 1489 (0.60%)	
occurrences (all)	11	9	
Floating patella			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	

Haemarthrosis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Joint dislocation		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Joint effusion		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Joint stiffness		
subjects affected / exposed	74 / 1449 (5.11%)	37 / 1489 (2.48%)
occurrences (all)	74	37
Joint swelling		
subjects affected / exposed	18 / 1449 (1.24%)	17 / 1489 (1.14%)
occurrences (all)	18	17
Neuropathic arthropathy		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Osteoarthritis		
subjects affected / exposed	67 / 1449 (4.62%)	53 / 1489 (3.56%)
occurrences (all)	67	53
Palindromic rheumatism		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Periarthritis		
subjects affected / exposed	9 / 1449 (0.62%)	4 / 1489 (0.27%)
occurrences (all)	9	4
Rheumatoid arthritis		
subjects affected / exposed	15 / 1449 (1.04%)	12 / 1489 (0.81%)
occurrences (all)	15	12
Rotator cuff syndrome		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Senile ankylosing vertebral hyperostosis		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Spinal osteoarthritis		
subjects affected / exposed	4 / 1449 (0.28%)	6 / 1489 (0.40%)
occurrences (all)	4	6
Spondylitis		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Temporomandibular joint syndrome		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Fibromyalgia		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Muscle atrophy		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Muscle spasms		
subjects affected / exposed	26 / 1449 (1.79%)	108 / 1489 (7.25%)
occurrences (all)	26	108
Myalgia		
subjects affected / exposed	124 / 1449 (8.56%)	106 / 1489 (7.12%)
occurrences (all)	124	106
Periodic limb movement disorder		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Torticollis		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Trismus		
subjects affected / exposed	3 / 1449 (0.21%)	1 / 1489 (0.07%)
occurrences (all)	3	1
Cervical spinal stenosis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Foot deformity		



subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Intervertebral disc compression		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Intervertebral disc disorder		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Intervertebral disc protrusion		
subjects affected / exposed	6 / 1449 (0.41%)	7 / 1489 (0.47%)
occurrences (all)	6	7
Lumbar spine flattening		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Sciatica		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Scoliosis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Axillary mass		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Back disorder		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Back pain		
subjects affected / exposed	82 / 1449 (5.66%)	101 / 1489 (6.78%)
occurrences (all)	82	101
Dupuytren's contracture		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Limb discomfort		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Musculoskeletal chest pain		

subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Musculoskeletal pain		
subjects affected / exposed	100 / 1449 (6.90%)	95 / 1489 (6.38%)
occurrences (all)	100	95
Musculoskeletal stiffness		
subjects affected / exposed	19 / 1449 (1.31%)	18 / 1489 (1.21%)
occurrences (all)	19	18
Neck mass		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Neck pain		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Pain in extremity		
subjects affected / exposed	101 / 1449 (6.97%)	80 / 1489 (5.37%)
occurrences (all)	101	80
Plantar fasciitis		
subjects affected / exposed	4 / 1449 (0.28%)	5 / 1489 (0.34%)
occurrences (all)	4	5
Bunion		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Bursitis		
subjects affected / exposed	2 / 1449 (0.14%)	11 / 1489 (0.74%)
occurrences (all)	2	11
Synovial cyst		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Cartilage injury		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Costochondritis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Tendonitis		

subjects affected / exposed	18 / 1449 (1.24%)	8 / 1489 (0.54%)	
occurrences (all)	18	8	
Tenosynovitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Trigger finger			
subjects affected / exposed	10 / 1449 (0.69%)	4 / 1489 (0.27%)	
occurrences (all)	10	4	
Breast cancer			
subjects affected / exposed	3 / 1449 (0.21%)	6 / 1489 (0.40%)	
occurrences (all)	3	6	
Infections and infestations			
Subacute sclerosing panencephalitis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Bacterial infection			
subjects affected / exposed	5 / 1449 (0.35%)	2 / 1489 (0.13%)	
occurrences (all)	5	2	
Breast cellulitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)	
occurrences (all)	0	2	
Folliculitis			
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)	
occurrences (all)	0	1	
Helicobacter gastritis			
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)	
occurrences (all)	1	0	
Helicobacter infection			
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)	
occurrences (all)	2	0	
Lyme disease			
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)	
occurrences (all)	0	3	

Staphylococcal infection		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Fungal infection		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Oral candidiasis		
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)
occurrences (all)	0	3
Pneumonia cryptococcal		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Vulvovaginal candidiasis		
subjects affected / exposed	9 / 1449 (0.62%)	42 / 1489 (2.82%)
occurrences (all)	9	42
Acute sinusitis		
subjects affected / exposed	1 / 1449 (0.07%)	3 / 1489 (0.20%)
occurrences (all)	1	3
Arthritis infective		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Breast abscess		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Bronchiectasis		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Chronic sinusitis		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Cystitis		
subjects affected / exposed	14 / 1449 (0.97%)	14 / 1489 (0.94%)
occurrences (all)	14	14
Diverticulitis		
subjects affected / exposed	4 / 1449 (0.28%)	5 / 1489 (0.34%)
occurrences (all)	4	5

Eye infection		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Furuncle		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Gastroenteritis		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Hordeolum		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Incision site infection		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Labyrinthitis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Liver abscess		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Localised infection		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Lower respiratory tract infection		
subjects affected / exposed	5 / 1449 (0.35%)	14 / 1489 (0.94%)
occurrences (all)	5	14
Lung infection		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Mastitis		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Otitis externa		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1

Otitis media		
subjects affected / exposed	4 / 1449 (0.28%)	4 / 1489 (0.27%)
occurrences (all)	4	4
Paronychia		
subjects affected / exposed	0 / 1449 (0.00%)	3 / 1489 (0.20%)
occurrences (all)	0	3
Pharyngitis		
subjects affected / exposed	2 / 1449 (0.14%)	7 / 1489 (0.47%)
occurrences (all)	2	7
Pneumonia		
subjects affected / exposed	5 / 1449 (0.35%)	0 / 1489 (0.00%)
occurrences (all)	5	0
Post procedural infection		
subjects affected / exposed	3 / 1449 (0.21%)	3 / 1489 (0.20%)
occurrences (all)	3	3
Respiratory tract infection		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Rhinitis		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Sepsis		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Sialoadenitis		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Sinusitis		
subjects affected / exposed	2 / 1449 (0.14%)	0 / 1489 (0.00%)
occurrences (all)	2	0
Skin infection		
subjects affected / exposed	1 / 1449 (0.07%)	4 / 1489 (0.27%)
occurrences (all)	1	4
Tonsillitis		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1

Tooth abscess		
subjects affected / exposed	5 / 1449 (0.35%)	7 / 1489 (0.47%)
occurrences (all)	5	7
Upper respiratory tract infection		
subjects affected / exposed	6 / 1449 (0.41%)	5 / 1489 (0.34%)
occurrences (all)	6	5
Urinary tract infection		
subjects affected / exposed	23 / 1449 (1.59%)	32 / 1489 (2.15%)
occurrences (all)	23	32
Wound infection		
subjects affected / exposed	1 / 1449 (0.07%)	1 / 1489 (0.07%)
occurrences (all)	1	1
Mycobacterial infection		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Tuberculosis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Toxoplasmosis		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hepatitis viral		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Herpes simplex		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Herpes zoster		
subjects affected / exposed	11 / 1449 (0.76%)	13 / 1489 (0.87%)
occurrences (all)	11	13
Influenza		
subjects affected / exposed	2 / 1449 (0.14%)	14 / 1489 (0.94%)
occurrences (all)	2	14
Post viral fatigue syndrome		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2

Vestibular neuronitis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	2 / 1489 (0.13%) 2	
Viral infection subjects affected / exposed occurrences (all)	7 / 1449 (0.48%) 7	8 / 1489 (0.54%) 8	
Metabolism and nutrition disorders			
Renal tubular acidosis subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Decreased appetite subjects affected / exposed occurrences (all)	10 / 1449 (0.69%) 10	6 / 1489 (0.40%) 6	
Increased appetite subjects affected / exposed occurrences (all)	2 / 1449 (0.14%) 2	0 / 1489 (0.00%) 0	
Weight fluctuation subjects affected / exposed occurrences (all)	6 / 1449 (0.41%) 6	2 / 1489 (0.13%) 2	
Bone metabolism disorder subjects affected / exposed occurrences (all)	0 / 1449 (0.00%) 0	1 / 1489 (0.07%) 1	
Osteopenia subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	0 / 1489 (0.00%) 0	
Osteoporosis subjects affected / exposed occurrences (all)	4 / 1449 (0.28%) 4	2 / 1489 (0.13%) 2	
Diabetic foot subjects affected / exposed occurrences (all)	1 / 1449 (0.07%) 1	1 / 1489 (0.07%) 1	
Fluid retention subjects affected / exposed occurrences (all)	3 / 1449 (0.21%) 3	5 / 1489 (0.34%) 5	
Hyperkalaemia			



subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hypokalaemia		
subjects affected / exposed	2 / 1449 (0.14%)	1 / 1489 (0.07%)
occurrences (all)	2	1
Hyponatraemia		
subjects affected / exposed	3 / 1449 (0.21%)	0 / 1489 (0.00%)
occurrences (all)	3	0
Diabetes mellitus		
subjects affected / exposed	21 / 1449 (1.45%)	13 / 1489 (0.87%)
occurrences (all)	21	13
Diabetes mellitus inadequate control		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Hypoglycaemia		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Type 1 diabetes mellitus		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Type 2 diabetes mellitus		
subjects affected / exposed	0 / 1449 (0.00%)	4 / 1489 (0.27%)
occurrences (all)	0	4
Haemochromatosis		
subjects affected / exposed	0 / 1449 (0.00%)	2 / 1489 (0.13%)
occurrences (all)	0	2
Iron deficiency anaemia		
subjects affected / exposed	2 / 1449 (0.14%)	3 / 1489 (0.20%)
occurrences (all)	2	3
Iron overload		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Hypercholesterolaemia		
subjects affected / exposed	47 / 1449 (3.24%)	11 / 1489 (0.74%)
occurrences (all)	47	11
Hyperlipidaemia		

subjects affected / exposed	3 / 1449 (0.21%)	8 / 1489 (0.54%)
occurrences (all)	3	8
Goitre		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Hypothyroidism		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Gout		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Folate deficiency		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Multi-vitamin deficiency		
subjects affected / exposed	1 / 1449 (0.07%)	0 / 1489 (0.00%)
occurrences (all)	1	0
Vitamin B12 deficiency		
subjects affected / exposed	0 / 1449 (0.00%)	1 / 1489 (0.07%)
occurrences (all)	0	1
Vitamin B6 deficiency		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2
Vitamin D deficiency		
subjects affected / exposed	1 / 1449 (0.07%)	2 / 1489 (0.13%)
occurrences (all)	1	2

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 February 2005	Transfer from CTC to CTA
23 September 2005	<ul style="list-style-type: none"> <li>- New steering committee members listed.</li> <li>- New GCP statement.</li> <li>- Clarification of roles of CR-UK and QM.</li> <li>- Addition of any previous breast cancer and history of gluten intolerance to exclusion criteria.</li> <li>- Clarification of acceptable management of menopausal symptoms.</li> <li>- Reference added to million women study.</li> <li>- Clarifications of lines of reporting for AEs and SAEs.</li> <li>- Clarification that the study nurse can consent patients in the study.</li> <li>- Clarification of requirements for blood samples and pathology specimens.</li> <li>- Development of new information flyer and poster on the DCIS arm of the trial.</li> </ul>
29 September 2006	<ul style="list-style-type: none"> <li>- Details of the new IBIS-II DCIS sites have been listed together with the names of the principal investigators.</li> <li>- A new joint patient information sheet (PIS) was developed for these patients who will be approached to enter the IBIS-II DCIS and/or BASO DCIS (DCIIS) trial. Each of these patients will now receive the IBIS-II DCIS PIS, the BASO DCIS PIS and the new joint IBIS-II/DCIS PIS.</li> <li>- Prof. Ian Weller has become chairman of the IBIS-II IDMC and Prof. Abdel Babiker has joined the IDMC.</li> </ul>
31 January 2007	<ul style="list-style-type: none"> <li>- The details of the new IBIS-II DCIS sites have been listed together with the names of the principal investigators.</li> <li>- The reference to 'bone pain' in section 10 of the IBIS-II DCIS PIS was clarified and changed to 'joint pain and stiffness' (I.e. Arthralgia).</li> <li>- The reference to CERES in section 2 was deleted.</li> <li>- Section 9 of IBIS-II DCIS PIS: 'What are the alternatives for diagnosis or treatment?' was reworded slightly: 'If you choose not to take part in the study, your treating clinician will advise whether you should take Tamoxifen or another appropriate treatment. Alternatively you may wish to have no additional treatment but rely on surgery and radiotherapy if recommended by your clinician.'</li> </ul>
21 May 2007	<ul style="list-style-type: none"> <li>- The details of the new IBIS-II DCIS sites have been listed together with the names of the principal investigators.</li> <li>- New eligibility criteria have been added to the protocol: 1) IBIS-I participants off trial therapy for at least 5 years; 2) Patients who have Paget's disease with underlying DCIS.</li> <li>- Carpal Tunnel Syndrome and ischaemic cardiovascular events have been added as a possible side effect of Anastrozole to the protocol and Carpal Tunnel Syndrome is now included in the PIS as a possible side effect.</li> <li>- Some of the members of the IDMC changed. These have been reflected in the protocol.</li> <li>- Notification of extension of recruitment to the end of 2010.</li> </ul>
30 April 2008	<ul style="list-style-type: none"> <li>- Creation of a questionnaire to follow up participants who are no longer on the trial. The questionnaire will only be sent out to participants who have agreed to be contacted by the IBIS-II CCO. It aims to record any medical conditions the women are experiencing and the severity of those conditions. It will also record any medication that the participants are taking.</li> </ul>

04 August 2008	<p>Women who have had a locally excised DCIS are only eligible if the Oestrogen Receptor and/or Progesterone Receptor (ER and/or PgR) status is known and is greater than or equal to 5% positive cells. The protocol previously stated that the ER and PgR status should be greater than 5% positive cells.</p> <p>Clarification of one of entry criteria. The protocol states that patients are eligible if they have had surgery to remove an ER or PgR +ve DCIS within the last six months. The protocol was previously unclear as to whether a patient was eligible for the trial six months from diagnosis or six months from surgery.</p> <p>Inclusion of a paragraph to say that where it is not possible for a patient to be randomized within this six month period between surgery for DCIS, due to unavailability of an appointment for baseline scans, the patient can join the trial provided that this is no longer than an additional three months. However, this must be authorised by the IBIS-II Central Coordinating Office (CCO). This has been added as we have found that many hospitals have long waiting lists for scans and the delays have had a knock-on effect in delaying randomization.</p> <p>Reference to the BASO DCIS II trial has been deleted as this trial is now closed.</p> <p>The protocol now states that two spinal x-rays in one lateral dimension are required to assess low trauma vertebral fractures. Due to a previous error the protocol had stated that only one x-ray was required.</p> <p>Clarified the issue of micro invasion; the protocol now states that patients with a multiple focus of micro invasion are eligible to join IBIS-II as long as each focus is less than 1mm in size. The protocol had previously stated that only a single focus of micro invasion was eligible for the trial.</p> <p>The protocol now states that the diagnosis of breast cancer is not an SAE as this is a study end point, included to comply with GCP.</p> <p>The end point of the trial has been defined as being the last participants' last visit.</p>
13 March 2009	<p>Changes to the age limits in the entry criteria for the DCIS trial in order to include more time to receive the test results for the trial. The age limits are currently 40-70 has been widened to +/-24 months of this range. However participants who are under 40 or over 70 can only enter on the agreement of the IBIS-II Steering Group co-chairmen.</p> <p>Also in order to include more time to receive the test results, an increase the time limit between scans and randomization. The entry criteria now states that: 1. If there is a delay in receiving the test results of a mammogram an extension of up to 6 months may be obtained with prior approval from one of the IBIS II Steering Group co-chairmen. 2. If there is a delay in receiving the test results of a DXA scan an extension of up to 6 months may be obtained with prior approval from one of the IBIS II Steering Group co-chairmen. 3. If there is a delay in receiving the test results of a spinal x-ray an extension of up to 12 months may be obtained with prior approval from one of the IBIS II Steering Group co-chairmen.</p> <p>Additional points added to the inclusion criteria: Patients who have had atypical hyperplasia or lobular carcinoma in-situ to be randomized into the DCIS trial plus 'In cases where the deep margin is less than 1mm, due to the proximity of the chest wall, the patient may be eligible if the clinicians involved in her care agree that the whole of the DCIS has been excised'. Removal of sentence from the exclusion criteria: If a participant is osteoporotic they can enter the trial as long as their T-score is more than minus four and they have no more than two low trauma vertebral fractures. In either case they must take bisphosphonate treatment and have regular DXA scans. The protocol had previously said 'The results of the scans must be provided to the trial, as for women in the IBIS-II Prevention bone sub-protocol.' Clarification to the entry criteria for the Quick score and H-score measures of ER/PR positivity.</p>
30 June 2009	<ul style="list-style-type: none"> <li>- Clarifications to the entry criteria of the DCIS protocol; osteoporotic women with T-scores greater than or equal to -4 (T-score <math>\geq</math> -4) are eligible for the DCIS trial.</li> <li>- Letter and reminder letter to accompany the IBIS-II annual questionnaire.</li> <li>- The IBIS-II CCO has been in contact with AstraZeneca regarding the distribution of updates of the Investigator Brochure (IB) to the IBIS-II sites. It has been agreed that instead of distributing hardcopy updates of the IB the IBIS-II team will now send electronic copies of the Summary of Product Characteristics (SmPC) instead.</li> </ul>
10 December 2009	<ul style="list-style-type: none"> <li>- New secondary labelling and distribution company</li> </ul>

11 January 2011	<ul style="list-style-type: none"> <li>- Addition of any history of lactose intolerance as an exclusion criterion.</li> <li>- Extension to the reporting of SAEs to cover the entire duration of the trial as requested by AZ.</li> <li>- Revision of the participant information sheet and consent forms specifically on frequency of mammogram and procedures for sending films, clarification that data may be obtained via NHS registries, and time to end of recruitment.</li> <li>- Revision of the post-treatment follow-up annual questionnaire.</li> <li>- Numerous non-substantial amendments to both the DCIS protocol and related study documents.</li> </ul>
28 February 2012	<ul style="list-style-type: none"> <li>- Notification to MHRA that Penn Pharmaceuticals will manufacture Tamoxifen placebo (replacing AZ)</li> </ul>
26 June 2014	<ul style="list-style-type: none"> <li>• Information on reporting of SAEs via data received from NHS registries,</li> <li>• Clarification of cancers that should not be reported as SAEs (but AEs),</li> <li>• A new common side effect which has been listed in the SmPC for Arimidex</li> <li>• A change of a Steering Committee member.</li> </ul>
30 June 2017	<p>Change in contact person for sponsor</p> <p>Protocol changes to reflect end of active treatment period (reduced sample size and supporting power calculation to meet primary objective, streamlined participant data collection questionnaires to focus on primary and unmet secondary objectives and simplified safety reporting procedures).</p> <p>Central storage of UK consent forms at trial coordinating office to support information requests for events identified by national registries (HES, ONS).</p> <p>Clarification of RSI control.</p> <p>Newsletter for IBIS-II participants with study updates.</p> <p>Update in trial oversight committee structures.</p> <p>Change in codebreak procedure to allow patient-requested codebreaks now active treatment period is complete.</p>
05 December 2019	<ul style="list-style-type: none"> <li>- Change of Trial Steering Committee members:</li> <li>- Closure of all UK sites - As part of a streamlining initiative started with amendment 52, to transfer follow up to NHS digital registries only</li> <li>- Reduced Safety reporting</li> <li>- Early closure of study in Italy</li> <li>- Clarification of consent process for collection and storage of patient identifiable information - Section added to revised protocol giving specific reference to ongoing section 251 CAG support</li> </ul>

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.

This CTIMP trial which recruited between 03 Mar 2003 and 08 Feb 2012 formally ended 6 months early on 31 May 2021 (early termination).  
Primary outcome analysis took place in 2016 (see publications). Data entry closed 31st May 2021.

Notes:

---

## Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26686313>