



Clinical trial results:

An Open-Label Extension Study of the Long-Term Safety of Pirfenidone in Patients with Idiopathic Pulmonary Fibrosis (IPF)

Summary

EudraCT number	2007-007800-13
Trial protocol	IE GB DE FR BE ES IT
Global end of trial date	11 February 2016

Results information

Result version number	v1 (current)
This version publication date	04 March 2017
First version publication date	04 March 2017

Trial information

Trial identification

Sponsor protocol code	GA29960
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00662038
WHO universal trial number (UTN)	-
Other trial identifiers	Alternate study identifier: PIPF-012

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Medical Communications, Hoffmann-La Roche, +1 800 8218590, genentech@druginfo.com
Scientific contact	Medical Communications, Hoffmann-La Roche, +1 800 8218590, genentech@druginfo.com

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	17 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2016
Global end of trial reached?	Yes
Global end of trial date	11 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The trial objective was to obtain additional safety data for pirfenidone 2403 mg/d in subjects with idiopathic pulmonary fibrosis (IPF) who completed either Study PIPF-004 or PIPF-006.

Protection of trial subjects:

Each subject, or the subject's representative, signed an informed consent form prior to screening.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 September 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	90 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 759
Country: Number of subjects enrolled	Australia: 63
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Brazil: 24
Country: Number of subjects enrolled	Canada: 32
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 43
Country: Number of subjects enrolled	Mexico: 16
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Peru: 36
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	United Kingdom: 10
Worldwide total number of subjects	1058
EEA total number of subjects	109

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	313
From 65 to 84 years	745
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1058 subjects enrolled from Studies PIPF-004/006/016.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Pirfenidone
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Arm description:

Pirfenidone, 2403 mg/d, administered as 801-mg doses, three times daily.

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

Dosage and administration details:

Pirfenidone, 2403 milligrams per day (mg/d), administered as 801 mg doses, three times daily.

Number of subjects in period 1	Pirfenidone
Started	1058
Completed	427
Not completed	631
Adverse event, serious fatal	95
Consent withdrawn by subject	83
Physician decision	19
Adverse event, non-fatal	358
Lung transplantation	44
Withdrawn consent	22
Reason not specified	3
Sponsor decision	1
Lost to follow-up	1
Continued treatment	5

Baseline characteristics

Reporting groups

Reporting group title	Pirfenidone
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Reporting group description:

Pirfenidone, 2403 mg/d, administered as 801-mg doses, three times daily.

Reporting group values	Pirfenidone	Total	
Number of subjects	1058	1058	
Age categorical			
Units: Subjects			
Adults (18-64 years)	313	313	
Elderly (From 65-84 years)	745	745	
Age Continuous			
Units: years			
arithmetic mean	68.5		
standard deviation	± 7.47	-	
Gender, Male/Female			
Units: Subjects			
Female	268	268	
Male	790	790	

End points

End points reporting groups

Reporting group title	Pirfenidone
Reporting group description: Pirfenidone, 2403 mg/d, administered as 801-mg doses, three times daily.	

Primary: Percentage of Subjects with Adverse Events

End point title	Percentage of Subjects with Adverse Events ^[1]
End point description: An adverse event defined as any unfavorable, harmful, or pathologic change in a research subject administered a pharmaceutical study treatment as indicated by physical signs, symptoms, and/or clinically significant laboratory abnormalities that occurred during the treatment and the post-treatment period, regardless of suspected cause.	
End point type	Primary
End point timeframe: 7.5 years	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive analysis only.

End point values	Pirfenidone			
Subject group type	Reporting group			
Number of subjects analysed	1058			
Units: percentage of subjects				
number (not applicable)	98			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

7.5 years

Adverse event reporting additional description:

Adverse events were recorded at every contact with the participant.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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Reporting groups

Reporting group title	Pirfenidone
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Reporting group description:

Pirfenidone, 2403 mg/d, administered as 801 mg doses, three times daily.

Serious adverse events	Pirfenidone		
Total subjects affected by serious adverse events			
subjects affected / exposed	571 / 1058 (53.97%)		
number of deaths (all causes)	231		
number of deaths resulting from adverse events	13		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Benign ovarian tumour			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder cancer recurrent			

subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Breast cancer				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Breast cancer in situ				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Breast cancer metastatic				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Bronchial carcinoma				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Burkitt's lymphoma				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic lymphocytic leukaemia				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	3 / 1058 (0.28%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Colon cancer metastatic				

subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric adenoma				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal carcinoma				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic neoplasm				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic neoplasm malignant				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal adenocarcinoma				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large cell carcinoma of the respiratory tract stage unspecified				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Lung adenocarcinoma				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma Stage IV				

subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung cancer metastatic				
subjects affected / exposed	6 / 1058 (0.57%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 3			
Lung neoplasm malignant				
subjects affected / exposed	8 / 1058 (0.76%)			
occurrences causally related to treatment / all	1 / 8			
deaths causally related to treatment / all	1 / 3			
Lung squamous cell carcinoma stage unspecified				
subjects affected / exposed	8 / 1058 (0.76%)			
occurrences causally related to treatment / all	1 / 9			
deaths causally related to treatment / all	0 / 1			
Lymphoma				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma Stage I				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant pleural effusion				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to bone				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Metastases to liver				

subjects affected / exposed	3 / 1058 (0.28%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer				
subjects affected / exposed	5 / 1058 (0.47%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer metastatic				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer Stage IV				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal adenocarcinoma metastatic				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal cancer metastatic				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ovarian cancer				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ovarian cancer recurrent				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma metastatic				

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Prostate cancer			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Prostate cancer metastatic			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Renal cancer			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sarcoma			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small cell carcinoma			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small cell lung cancer stage unspecified			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Squamous cell carcinoma			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Air embolism			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Aortic aneurysm			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Aortic stenosis			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Arterial occlusive disease			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	7 / 1058 (0.66%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Arteriosclerosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hypertension			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolism venous			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			

subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	7 / 1058 (0.66%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Peripheral vascular disorder			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vasculitis necrotising			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	15 / 1058 (1.42%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 0		
Death			

subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Hypothermia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multi-organ failure			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	6 / 1058 (0.57%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anti-neutrophil cytoplasmic antibody positive vasculitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Polyarteritis nodosa			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Endometriosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endosalpingiosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Female genital tract fistula			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic floor muscle weakness			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatitis			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute respiratory failure			
subjects affected / exposed	30 / 1058 (2.84%)		
occurrences causally related to treatment / all	5 / 30		
deaths causally related to treatment / all	2 / 11		
Alveolitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			

subjects affected / exposed	8 / 1058 (0.76%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Haemothorax			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	17 / 1058 (1.61%)		
occurrences causally related to treatment / all	1 / 18		
deaths causally related to treatment / all	1 / 4		
Idiopathic pulmonary fibrosis			
subjects affected / exposed	230 / 1058 (21.74%)		
occurrences causally related to treatment / all	9 / 276		
deaths causally related to treatment / all	2 / 133		
Increased bronchial secretion			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Lung disorder			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nasal discomfort			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleurisy			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumomediastinum			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	8 / 1058 (0.76%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 1		
Pneumonitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	8 / 1058 (0.76%)		
occurrences causally related to treatment / all	2 / 12		
deaths causally related to treatment / all	0 / 0		
Pneumothorax spontaneous tension			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary arterial hypertension			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	19 / 1058 (1.80%)		
occurrences causally related to treatment / all	3 / 20		
deaths causally related to treatment / all	0 / 0		
Pulmonary cavitation			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary haemorrhage			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	11 / 1058 (1.04%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 2		
Pulmonary mass			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory failure			
subjects affected / exposed	29 / 1058 (2.74%)		
occurrences causally related to treatment / all	4 / 29		
deaths causally related to treatment / all	1 / 18		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			

subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Mycobacteria blood test positive			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Panel-reactive antibody increased			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pulmonary arterial pressure increased			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Troponin increased			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour marker increased			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Burns second degree			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cervical vertebral fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device lead damage			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug toxicity			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Extradural haematoma			

subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Failure of implant				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	5 / 1058 (0.47%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fractured coccyx				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	4 / 1058 (0.38%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Incisional hernia, obstructive			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Patella fracture			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Post procedural complication			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation pneumonitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal haematoma			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal injury			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skeletal injury			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin laceration			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			

subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Spinal cord injury			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sternal fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Struck by lightning			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ulna fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Gastrointestinal arteriovenous malformation			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	7 / 1058 (0.66%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	12 / 1058 (1.13%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 1		
Acute right ventricular failure			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	6 / 1058 (0.57%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Aortic valve stenosis			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Arteriosclerosis coronary artery			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	26 / 1058 (2.46%)		
occurrences causally related to treatment / all	1 / 32		
deaths causally related to treatment / all	0 / 1		
Atrial flutter			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Atrial tachycardia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	5 / 1058 (0.47%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	9 / 1058 (0.85%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 6		
Cardiac failure			

subjects affected / exposed	5 / 1058 (0.47%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	12 / 1058 (1.13%)		
occurrences causally related to treatment / all	1 / 19		
deaths causally related to treatment / all	1 / 2		
Cardiomyopathy			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cor pulmonale			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	20 / 1058 (1.89%)		
occurrences causally related to treatment / all	0 / 20		
deaths causally related to treatment / all	0 / 0		
Coronary artery dissection			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery occlusion			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Heart valve incompetence			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left ventricular dysfunction			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left ventricular failure			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	7 / 1058 (0.66%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	1 / 3		
Myocardial ischaemia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Palpitations			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Right ventricular dysfunction			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Right ventricular failure			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Sick sinus syndrome			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Sinus bradycardia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular extrasystoles			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Anoxic encephalopathy			

subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Brain stem infarction				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Carotid artery stenosis				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Central nervous system lesion				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haematoma				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral thrombosis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				

subjects affected / exposed	14 / 1058 (1.32%)			
occurrences causally related to treatment / all	3 / 16			
deaths causally related to treatment / all	1 / 4			
Chronic inflammatory demyelinating polyradiculoneuropathy				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	3 / 1058 (0.28%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Demyelinating polyneuropathy				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Embolic stroke				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoaesthesia				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Mononeuropathy multiplex			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraparesis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	20 / 1058 (1.89%)		
occurrences causally related to treatment / all	2 / 26		
deaths causally related to treatment / all	0 / 0		
Syncope vasovagal			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tension headache			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thalamic infarction			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	8 / 1058 (0.76%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 1058 (0.47%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Coagulopathy			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic anaemia			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Iron deficiency anaemia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vertigo positional			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eye disorder			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Colitis ischaemic			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colonic fistula			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Colonic polyp				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulum				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	5 / 1058 (0.47%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal necrosis				

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia strangulated			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Intra-abdominal haematoma			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jejunal perforation			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Obstruction gastric			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal perforation			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal polyp			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Small intestinal perforation			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia, obstructive			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bile duct stenosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bile duct stone			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Biliary dyskinesia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			

subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Cholecystitis chronic			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoaesthesia facial			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Photosensitivity reaction			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Calculus urinary			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Glomerulonephritis rapidly progressive			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	6 / 1058 (0.57%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Renal cyst			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Renal failure acute			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal mass			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Costochondritis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc degeneration			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc disorder			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscle spasms			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neck pain			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	7 / 1058 (0.66%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Osteoporosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Polymyalgia rheumatica			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal column stenosis			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abscess intestinal			

subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute sinusitis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bacterial abscess central nervous system				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bartonellosis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	32 / 1058 (3.02%)			
occurrences causally related to treatment / all	0 / 38			
deaths causally related to treatment / all	0 / 0			
Bronchitis viral				

subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bursitis infective				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Campylobacter intestinal infection				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Candidiasis				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	3 / 1058 (0.28%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cellulitis staphylococcal				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridial infection				

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis enterococcal			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterococcal bacteraemia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterocolitis infectious			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fungal oesophagitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			

subjects affected / exposed	3 / 1058 (0.28%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster oticus				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	7 / 1058 (0.66%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Liver abscess				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	4 / 1058 (0.38%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	1 / 1			
Lower respiratory tract infection				
subjects affected / exposed	4 / 1058 (0.38%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection bacterial				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				

subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Lung infection pseudomonal				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jiroveci pneumonia				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Pneumonia				
subjects affected / exposed	90 / 1058 (8.51%)			
occurrences causally related to treatment / all	7 / 104			
deaths causally related to treatment / all	1 / 10			
Pneumonia bacterial				
subjects affected / exposed	2 / 1058 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia herpes viral				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia influenzal				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonia pneumococcal				
subjects affected / exposed	1 / 1058 (0.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				

subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia staphylococcal			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pneumonia streptococcal			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative abscess			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomembranous colitis			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	3 / 1058 (0.28%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	8 / 1058 (0.76%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Dehydration			

subjects affected / exposed	6 / 1058 (0.57%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypochloraemia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	2 / 1058 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	4 / 1058 (0.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Hypovolaemia			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	1 / 1058 (0.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pirfenidone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1027 / 1058 (97.07%)		
Investigations			
Weight decreased			
subjects affected / exposed	153 / 1058 (14.46%)		
occurrences (all)	173		
Vascular disorders			
Hypertension			
subjects affected / exposed	71 / 1058 (6.71%)		
occurrences (all)	72		
Nervous system disorders			
Dizziness			
subjects affected / exposed	176 / 1058 (16.64%)		
occurrences (all)	225		
Headache			
subjects affected / exposed	157 / 1058 (14.84%)		
occurrences (all)	248		
Syncope			
subjects affected / exposed	55 / 1058 (5.20%)		
occurrences (all)	65		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	128 / 1058 (12.10%)		
occurrences (all)	159		
Fatigue			
subjects affected / exposed	210 / 1058 (19.85%)		
occurrences (all)	251		
Asthenia			
subjects affected / exposed	65 / 1058 (6.14%)		
occurrences (all)	72		
Chest pain			
subjects affected / exposed	64 / 1058 (6.05%)		
occurrences (all)	76		
Pyrexia			

subjects affected / exposed occurrences (all)	60 / 1058 (5.67%) 78		
Eye disorders Cataract subjects affected / exposed occurrences (all)	53 / 1058 (5.01%) 67		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	60 / 1058 (5.67%) 72		
Abdominal pain upper subjects affected / exposed occurrences (all)	66 / 1058 (6.24%) 84		
Constipation subjects affected / exposed occurrences (all)	118 / 1058 (11.15%) 142		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	102 / 1058 (9.64%) 112		
Diarrhoea subjects affected / exposed occurrences (all)	242 / 1058 (22.87%) 357		
Dyspepsia subjects affected / exposed occurrences (all)	126 / 1058 (11.91%) 150		
Stomach discomfort subjects affected / exposed occurrences (all)	53 / 1058 (5.01%) 73		
Vomiting subjects affected / exposed occurrences (all)	122 / 1058 (11.53%) 172		
Nausea subjects affected / exposed occurrences (all)	305 / 1058 (28.83%) 431		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	330 / 1058 (31.19%) 435		
Dyspnoea exertional subjects affected / exposed occurrences (all)	68 / 1058 (6.43%) 69		
Dyspnoea subjects affected / exposed occurrences (all)	325 / 1058 (30.72%) 412		
Epistaxis subjects affected / exposed occurrences (all)	64 / 1058 (6.05%) 84		
Idiopathic pulmonary fibrosis subjects affected / exposed occurrences (all)	221 / 1058 (20.89%) 271		
Hypoxia subjects affected / exposed occurrences (all)	73 / 1058 (6.90%) 79		
Productive cough subjects affected / exposed occurrences (all)	62 / 1058 (5.86%) 75		
Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	71 / 1058 (6.71%) 86		
Nasal congestion subjects affected / exposed occurrences (all)	56 / 1058 (5.29%) 64		
Pulmonary hypertension subjects affected / exposed occurrences (all)	123 / 1058 (11.63%) 128		
Skin and subcutaneous tissue disorders Photosensitivity reaction subjects affected / exposed occurrences (all)	74 / 1058 (6.99%) 98		
Pruritus			

subjects affected / exposed	71 / 1058 (6.71%)		
occurrences (all)	82		
Rash			
subjects affected / exposed	156 / 1058 (14.74%)		
occurrences (all)	230		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	84 / 1058 (7.94%)		
occurrences (all)	89		
Insomnia			
subjects affected / exposed	111 / 1058 (10.49%)		
occurrences (all)	121		
Depression			
subjects affected / exposed	82 / 1058 (7.75%)		
occurrences (all)	85		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	146 / 1058 (13.80%)		
occurrences (all)	178		
Arthralgia			
subjects affected / exposed	89 / 1058 (8.41%)		
occurrences (all)	119		
Pain in extremity			
subjects affected / exposed	67 / 1058 (6.33%)		
occurrences (all)	82		
Infections and infestations			
Bronchitis			
subjects affected / exposed	254 / 1058 (24.01%)		
occurrences (all)	447		
Influenza			
subjects affected / exposed	75 / 1058 (7.09%)		
occurrences (all)	94		
Lower respiratory tract infection			
subjects affected / exposed	67 / 1058 (6.33%)		
occurrences (all)	123		

Respiratory tract infection subjects affected / exposed occurrences (all)	57 / 1058 (5.39%) 69		
Nasopharyngitis subjects affected / exposed occurrences (all)	202 / 1058 (19.09%) 359		
Pneumonia subjects affected / exposed occurrences (all)	88 / 1058 (8.32%) 107		
Urinary tract infection subjects affected / exposed occurrences (all)	103 / 1058 (9.74%) 190		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	295 / 1058 (27.88%) 522		
Sinusitis subjects affected / exposed occurrences (all)	130 / 1058 (12.29%) 218		
Metabolism and nutrition disorders			
Anorexia subjects affected / exposed occurrences (all)	120 / 1058 (11.34%) 136		
Decreased appetite subjects affected / exposed occurrences (all)	95 / 1058 (8.98%) 103		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2010	Revised duration of treatment period; clarified dose escalation for subjects who required dose reduction while participating in Study PIPF-004; clarified exclusion criteria for QT corrected for heart rate using Bazett's method (QTcB); incorporated updated background information; revised windows for post-treatment follow-up visit and collection of concomitant medications; revised requirements for early withdrawal from study visit; corrected required visits for subjects who required restart visits.
07 October 2011	Allowed subjects from additional qualifying InterMune clinical studies to enroll (previously limited to subjects from Studies PIPF-004/006); eliminated efficacy assessments as of 15 May 2012; simplified and clarified the safety assessments as of 15 May 2012, as follows: revised prohibited prior and concomitant medications; eliminated exclusion criteria related to liver tests and electrocardiogram (ECG) results; eliminated subject diary; clarified dose-escalation guidelines, and revised dose-modification, interruption, and restart guidelines; clarified requirements for pre-restart and restart visits; updated adverse event reporting guidelines.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported