Clinical trial results:
An open-label, multicenter, expanded access study of INC424 for patients with primary myelofibrosis (PMF) of post polycythemia vera myelofibrosis (PPV MF) or post-essential thrombocythemia myelofibrosis (PET-MF)

Summary

EudraCT number	2010-024473-39
Trial protocol	AT CZ BE DE ES GR HU PT SK PL IT IE
Global end of trial date	26 January 2017

Results information

Result version number	v1 (current)
This version publication date	11 February 2018
First version publication date	11 February 2018

Trial information

Trial identification

Sponsor protocol code	CINC424A2401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01493414
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

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	26 January 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To collect additional safety data of ruxolitinib in patients with PMF, PPV-MF, or PET-MF who have either received prior treatment with commercially available agents, investigational drug or who have never received treatment.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 August 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Algeria: 19
Country: Number of subjects enrolled	Argentina: 42
Country: Number of subjects enrolled	Brazil: 104
Country: Number of subjects enrolled	Canada: 53
Country: Number of subjects enrolled	Colombia: 18
Country: Number of subjects enrolled	Mexico: 26
Country: Number of subjects enrolled	Poland: 39
Country: Number of subjects enrolled	Portugal: 27
Country: Number of subjects enrolled	Slovakia: 17
Country: Number of subjects enrolled	Spain: 363
Country: Number of subjects enrolled	Austria: 31
Country: Number of subjects enrolled	Belgium: 55
Country: Number of subjects enrolled	Czech Republic: 12
Country: Number of subjects enrolled	Germany: 376
Country: Number of subjects enrolled	Greece: 17
Country: Number of subjects enrolled	Hungary: 26
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Italy: 861
Country: Number of subjects enrolled	Luxembourg: 6

Country: Number of subjects enrolled	Morocco: 3
Country: Number of subjects enrolled	Russian Federation: 34
Country: Number of subjects enrolled	Saudi Arabia: 8
Country: Number of subjects enrolled	South Africa: 29
Country: Number of subjects enrolled	Thailand: 19
Country: Number of subjects enrolled	Tunisia: 27
Country: Number of subjects enrolled	Israel: 20
Worldwide total number of subjects	2233
EEA total number of subjects	1831

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)	899
From 65 to 84 years	1312
85 years and over	22

Subject disposition

Recruitment

Recruitment details:

This was an expanded access study intended to provide an access path to ruxolitinib for patients with Myelofibrosis (MF) and to allow for collection of additional safety and efficacy data for ruxolitinib.

Pre-assignment

Screening details:

All patients were to be screened for inclusion and exclusion criteria within 28 days prior to the first dose of ruxolitinib.

Period 1

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

Arms

Arm title	INC424

Arm description:

5 - 25 mg twice a day (BID)
INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Arm type	Experimental
Investigational medicinal product name	INC424
Investigational medicinal product code	
Other name	Ruxolitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Number of subjects in period 1	INC424
Started	2233
Completed	1283
Not completed	950
Physician decision	93
Consent withdrawn by subject	79
Disease progression	204
Adverse Event	405
Death	101

Administrative problems	25
Lost to follow-up	16
Protocol deviation	27

Baseline characteristics

Reporting groups	
Reporting group title	INC424

Reporting group description:

5 - 25 mg twice a day (BID)
INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Reporting group values	INC424	Total	
Number of subjects	2233	2233	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	899	899	
From 65-84 years	1312	1312	
85 years and over	22	22	
Age continuous Units: years			
arithmetic mean	65.6		
standard deviation	± 10.50	-	
Gender categorical Units: Subjects			
Female	1016	1016	
Male	1217	1217	
ECOG score Units: Subjects			
00	1061	1061	
01	960	960	
02	197	197	
03	1	1	
04	0	0	
Missing	14	14	

End points

End points reporting groups

Reporting group title	INC424

Reporting group description:

5 - 25 mg twice a day (BID)
INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Subject analysis set title	INC424 - Responders
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Responders with spleen length between 5 and 10 cm=non palpable spleen. Responders with spleen length more than 10 cm=Spleen reduction of 50% from baseline.

5 - 25 mg twice a day (BID) INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Subject analysis set title	INC424 - Stable Disease
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with Stable Disease with spleen length between 5 and 10 cm=does not meet criteria for response or disease progression.
Participants with Stable Disease with spleen length more than 10 cm=does not meet criteria for response or disease progression.

5 - 25 mg twice a day (BID) INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Subject analysis set title	INC424 - Progressive Disease
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with Progressive Disease with spleen length between 5 and 10 cm=increase of 100% from baseline in spleen length.
Participants with Progressive Disease with spleen length more than 10 cm=increase of 50% from baseline in spleen length.

5 - 25 mg twice a day (BID) INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Subject analysis set title	INC424 - Missing
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Missing values.

5 - 25 mg twice a day (BID) INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Primary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) up to 5 Years

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) up to 5 Years[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical trial participant regardless of causal relationship to study drug and regardless whether study drug has been administered. A serious adverse event (SAE) is any untoward medical occurrence or effect that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in

persistent or significant disability / incapacity, is a congenital anomaly / birth defect or is medically important due to other reasons than the above mentioned criteria. A non-serious AE is any AE that does not meet the criteria above.
The occurrence of adverse events may be volunteered by the patient or obtained by non-directive questioning at each visit during the study or through physical examination, laboratory test, or other assessments.

End point type	Primary

End point timeframe:

Baseline up to approximately 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: No statistical analyses were completed for this primary end point.

End point values	INC424			
Subject group type	Reporting group			
Number of subjects analysed	2233[2]			
Units: Count of Participants				
number (not applicable)				
Adverse Events	2153			
Serious adverse events	830			

Notes:

[2] - Safety set-all patients who received one dose of study drug and one post-baseline safety assessment

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With at Least 50% Reduction in Spleen Length

End point title	Percentage of Participants With at Least 50% Reduction in Spleen Length

End point description:

Spleen length was assessed by manual palpation. Assessment of spleen response was repeated until early discontinuation of the study drug and also at study completion (28 days post end of treatment visit).

End point type	Secondary

End point timeframe:

Baseline up to approximately 5 years

End point values	INC424			
Subject group type	Reporting group			
Number of subjects analysed	2049[3]			
Units: participants				
number (confidence interval 95%)	71.7 (69.7 to 73.7)			

Notes:

[3] - Full analysis set includes all patients who received at least one administration of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (BOR) up to 5 Years

End point title	Best Overall Response (BOR) up to 5 Years

End point description:

Overall response is analyzed using the spleen response, as assessed by the investigator and also by deriving the response using International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) criteria.
Subjects with spleen length of less than 5 cm are not evaluable and do not appear in table.

End point type	Secondary

End point timeframe:

Baseline up to approximately 5 years

End point values	INC424 - Responders	INC424 - Stable Disease	INC424 - Progressive Disease	INC424 - Missing
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2233[4]	2233[5]	2233[6]	2233[7]
Units: Participants				
number (not applicable)				
Between 5 and 10 cm (N = 765)	421	334	1	9
More than 10 cm (N = 1224)	742	463	0	19

Notes:

[4] - FAS

[5] - FAS

[6] - FAS

[7] - FAS

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Improvement in FACT-Lym, FACIT-Fatigue Score and ECOG Performance Status

End point title	Time to First Improvement in FACT-Lym, FACIT-Fatigue Score and ECOG Performance Status

End point description:

End point type	Secondary

End point timeframe:

Baseline up to approximately 5 years

End point values	INC424			
Subject group type	Reporting group			
Number of subjects analysed	2233[8]			
Units: weeks				
median (confidence interval 95%)				
FACT-Lym Total score median time to improvement	10.9 (5.1 to 11.6)			
FACIT – Fatigue score median time to improvement	4.6 (4.4 to 4.6)			
ECOG score median time to improvement	63.1 (61.1 to 65.0)			

Notes:

[8] - Full analysis set includes all patients who received at least one administration of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Eastern Cooperative Oncology Group (ECOG) Performance Status up to 5 Years

End point title	Change in Eastern Cooperative Oncology Group (ECOG) Performance Status up to 5 Years

End point description:

ECOG Performance Score has 4 grades. 0 = Fully active, able to carry out all pre-disease activities; 1 = Restricted in strenuous activity but ambulatory and able to carry out work of light or sedentary nature; 2 = Ambulatory and capable of all self-care but unable to carry out work activities. Active about 50% of waking hours; 3 = Capable of limited self-care, confined to bed/chair more than 50% of waking hours; 4 = Completely disabled; cannot carry on self-care. Totally confined to bed/chair.

End point type	Secondary

End point timeframe:

Baseline up to approximately 5 years

End point values	INC424			
Subject group type	Reporting group			
Number of subjects analysed	2233[9]			
Units: participants				
number (not applicable)				
Baseline - Grade 0:Worst post-baseline: Grade 0	598			
Baseline - Grade 0:Worst post-baseline: Grade 1	377			
Baseline - Grade 0:Worst post-baseline: Grade 2	62			
Baseline - Grade 0:Worst post-baseline: Grade 3	12			
Baseline - Grade 0:Worst post-baseline: Grade 4	7			

Baseline - Grade 0:Worst post-baseline: Grade 5	0			
Baseline - Grade 0:Worst post-baseline: Missing	5			
Baseline - Grade 1:Worst post-baseline: Grade 0	89			
Baseline - Grade 1:Worst post-baseline: Grade 1	629			
Baseline - Grade 1:Worst post-baseline: Grade 2	187			
Baseline - Grade 1:Worst post-baseline: Grade 3	26			
Baseline - Grade 1:Worst post-baseline: Grade 4	12			
Baseline - Grade 1:Worst post-baseline: Grade 5	1			
Baseline - Grade 1:Worst post-baseline: Missing	16			
Baseline - Grade 2:Worst post-baseline: Grade 0	3			
Baseline - Grade 2:Worst post-baseline: Grade 1	43			
Baseline - Grade 2:Worst post-baseline: Grade 2	111			
Baseline - Grade 2:Worst post-baseline: Grade 3	20			
Baseline - Grade 2:Worst post-baseline: Grade 4	12			
Baseline - Grade 2:Worst post-baseline: Grade 5	1			
Baseline - Grade 2:Worst post-baseline: Missing	7			
Baseline - Grade 3:Worst post-baseline: Grade 0	0			
Baseline - Grade 3:Worst post-baseline: Grade 1	0			
Baseline - Grade 3:Worst post-baseline: Grade 2	0			
Baseline - Grade 3:Worst post-baseline: Grade 3	1			
Baseline - Grade 3:Worst post-baseline: Grade 4	0			
Baseline - Grade 3:Worst post-baseline: Grade 5	0			
Baseline - Grade 3:Worst post-baseline: Missing	0			
Baseline - Grade 4:Worst post-baseline: Grade 0	0			
Baseline - Grade 4:Worst post-baseline: Grade 1	0			
Baseline - Grade 4:Worst post-baseline: Grade 2	0			
Baseline - Grade 4:Worst post-baseline: Grade 3	0			
Baseline - Grade 4:Worst post-baseline: Grade 4	0			
Baseline - Grade 4:Worst post-baseline: Grade 5	0			
Baseline - Grade 4:Worst post-baseline: Missing	0			
Baseline - Missing:Worst post-baseline: Grade 0	1			

Baseline - Missing:Worst post-baseline: Grade 1	8			
Baseline - Missing:Worst post-baseline: Grade 2	4			
Baseline - Missing:Worst post-baseline: Grade 3	1			
Baseline - Missing:Worst post-baseline: Grade 4	0			
Baseline - Missing:Worst post-baseline: Grade 5	0			
Baseline - Missing:Worst post-baseline: Missing	0			

Notes:

[9] - FAS
N= G0 1061, Baseline - G1 960,Baseline - G2 197, Baseline - G3 1, Baseline - G4 0, GMissing 14

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Functional Assessment of Cancer Therapy (FACT-TOI, FACT-G) and FACT-Lymphoma (FACT-Lym) Total Scores up to Week 48

End point title	Change in Functional Assessment of Cancer Therapy (FACT-TOI, FACT-G) and FACT-Lymphoma (FACT-Lym) Total Scores up to Week 48

End point description:

The FACT-Lym questionnaire consists of a total of 42 questions divided between five subscales (i.e., physical well-being, social/family well-being, emotional well-being, functional well-being and lymphoma subscale) which in turn contribute to three total sum scores, namely FACT-Lym Trial Outcome Index (TOI), FACT-General (FACT-G) total score and FACT- Lym total score.

End point type	Secondary

End point timeframe:

Baseline to Week 48

End point values	INC424			
Subject group type	Reporting group			
Number of subjects analysed	2233[10]			
Units: scores on a scale				
arithmetic mean (standard deviation)				
FACT-Lymphoma Baseline	42.3 (± 10.20)			
FACT-Lymphoma Week 48	47.9 (± 8.47)			
FACT-Lymphoma TOI Baseline	77.9 (± 18.99)			
FACT-Lymphoma TOI Week 48	86.8 (± 16.42)			
FACT-Lymphoma total score Baseline	113.9 (± 24.01)			
FACT-Lymphoma total score Week 48	123.3 (± 22.34)			
FACT-G Baseline	71.6 (± 15.98)			
FACT-G Week 48	75.5 (± 15.59)			

Notes:

[10] - FAS; N= 2065, 952, 2034, 940, 2029, 937, 2050, 950

Statistical analyses

No statistical analyses for this end point

Secondary: Medical Resource Utilization up to 5 Years

End point title	Medical Resource Utilization up to 5 Years

End point description:

Percentage of patients requiring medical resources (blood transfusions, hospitalization, emergency room visits, general practitioners or specialists consultations, urgent care or splenic irradiation) up to 5 years.

End point type	Secondary

End point timeframe:

Baseline up to approximately 5 years.

End point values	INC424			
Subject group type	Reporting group			
Number of subjects analysed	2233[11]			
Units: participants				
number (not applicable)				
Baseline- Dependency vs End of Study - Dependency	129			
Baseline- Dependency vs End of Study- Independency	29			
Baseline- Independency vs End of Study-Dependency	480			
Baseline-Independency vs End of Study- Idependency	1595			

Notes:

[11] - FAS
Baseline- Dependency n= 158
Baseline- Independency n =2075

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected up to 24-months after last patient first visit (LPFV) for each participant, up to approximately 5 years.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	INC424

Reporting group description:

5 - 25 mg twice a day (BID)
INC424: All patients enrolled into the study will receive INC424 (ruxolitinib). Starting dose is based on baseline platelet counts, with doses ranging from 5 to 20 mg twice a day. No INC424 dose will exceed 25 mg BID orally.

Serious adverse events	INC424		
Total subjects affected by serious adverse events			
subjects affected / exposed	830 / 2233 (37.17%)		
number of deaths (all causes)	205		
number of deaths resulting from adverse events	20		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute leukaemia			
subjects affected / exposed	13 / 2233 (0.58%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 2		
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Acute myeloid leukaemia			
subjects affected / exposed	18 / 2233 (0.81%)		
occurrences causally related to treatment / all	2 / 18		
deaths causally related to treatment / all	0 / 4		
B-cell lymphoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	10 / 2233 (0.45%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 0		
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blast cell crisis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chloroma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholangiocarcinoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Chronic lymphocytic leukaemia			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chronic myeloid leukaemia			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic myeloid leukaemia transformation			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Chronic myelomonocytic leukaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal adenocarcinoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leukaemia			
subjects affected / exposed	7 / 2233 (0.31%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 1		
Lung neoplasm malignant			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Lymphangioma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to liver			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to lung			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Monoclonal gammopathy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myelofibrosis			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Myeloid metaplasia			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Neoplasm			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Neoplasm skin			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Neuroendocrine carcinoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuroendocrine tumour			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-Hodgkin's lymphoma			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Pelvic neoplasm			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Prostate cancer			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Rectal adenocarcinoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Second primary malignancy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Squamous cell carcinoma			
subjects affected / exposed	9 / 2233 (0.40%)		
occurrences causally related to treatment / all	1 / 14		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	6 / 2233 (0.27%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the vagina			

subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transitional cell carcinoma				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour thrombosis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Aortic rupture				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arterial disorder				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Arterial haemorrhage				

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Circulatory collapse			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	10 / 2233 (0.45%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 1		
Embolism			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
subjects affected / exposed	9 / 2233 (0.40%)		
occurrences causally related to treatment / all	2 / 10		
deaths causally related to treatment / all	0 / 0		
Hyperaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			

subjects affected / exposed	7 / 2233 (0.31%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Pallor			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peripheral artery occlusion			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery stenosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Phlebitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis superficial			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			
Stem cell transplant			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	14 / 2233 (0.63%)		
occurrences causally related to treatment / all	4 / 15		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	12 / 2233 (0.54%)		
occurrences causally related to treatment / all	1 / 12		
deaths causally related to treatment / all	1 / 10		
Disease progression			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Drug withdrawal syndrome			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Face oedema			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Fatigue				
subjects affected / exposed	11 / 2233 (0.49%)			
occurrences causally related to treatment / all	1 / 13			
deaths causally related to treatment / all	0 / 1			
Gait disturbance				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	19 / 2233 (0.85%)			
occurrences causally related to treatment / all	2 / 19			
deaths causally related to treatment / all	0 / 1			
Generalised oedema				
subjects affected / exposed	5 / 2233 (0.22%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Hernia				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperpyrexia				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	11 / 2233 (0.49%)			
occurrences causally related to treatment / all	3 / 11			
deaths causally related to treatment / all	1 / 7			
Nodule				

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	10 / 2233 (0.45%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral swelling			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Polyp			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudocyst			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	79 / 2233 (3.54%)		
occurrences causally related to treatment / all	11 / 85		
deaths causally related to treatment / all	0 / 1		
Sudden death			

subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immunosuppression			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cervical dysplasia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Menometrorrhagia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Postmenopausal haemorrhage				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostatitis				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Testicular pain				
subjects affected / exposed	1 / 2233 (0.04%)			
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	4 / 2233 (0.18%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	1 / 2			
Acute respiratory distress syndrome				
subjects affected / exposed	7 / 2233 (0.31%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 4			
Acute respiratory failure				
subjects affected / exposed	7 / 2233 (0.31%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 1			
Alveolitis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Asthma				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Bronchospasm				
subjects affected / exposed	3 / 2233 (0.13%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	3 / 2233 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Chronic respiratory failure				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	6 / 2233 (0.27%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	36 / 2233 (1.61%)			
occurrences causally related to treatment / all	7 / 39			
deaths causally related to treatment / all	0 / 1			
Emphysema				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	10 / 2233 (0.45%)			
occurrences causally related to treatment / all	1 / 10			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	4 / 2233 (0.18%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Haemothorax				

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydrothorax			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infiltration			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal pain			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	13 / 2233 (0.58%)		
occurrences causally related to treatment / all	1 / 13		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	3 / 6		
deaths causally related to treatment / all	0 / 1		
Pneumothorax			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Productive cough			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	18 / 2233 (0.81%)		
occurrences causally related to treatment / all	2 / 18		
deaths causally related to treatment / all	1 / 5		
Pulmonary haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	2 / 9		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 2		
Respiratory distress			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	26 / 2233 (1.16%)		
occurrences causally related to treatment / all	2 / 27		
deaths causally related to treatment / all	0 / 7		
Thoracic haemorrhage			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety disorder			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Disorientation			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device leakage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			

Bile duct stone			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Biliary colic			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholangitis chronic			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatorenal syndrome			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Portal hypertension			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Portal vein thrombosis			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blast cell count increased			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood lactate dehydrogenase increased			

subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Body temperature increased				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cardioactive drug level increased				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ejection fraction decreased				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram QT prolonged				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram T wave abnormal				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram T wave amplitude increased				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epstein-Barr virus antigen positive				

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical condition abnormal			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Haemoglobin decreased			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Heart rate irregular			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lipase increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myeloblast count increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Portal vein pressure increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sensory level abnormal			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Troponin I increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
White blood cell count increased			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Arterial injury			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain contusion			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Craniocerebral injury			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Crush injury			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Face injury			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Facial bones fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	6 / 2233 (0.27%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			

subjects affected / exposed	6 / 2233 (0.27%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Foot fracture			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Fractured sacrum			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Heart injury			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Joint injury			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Limb injury			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Patella fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Splenic injury			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Splenic rupture			
subjects affected / exposed	7 / 2233 (0.31%)		
occurrences causally related to treatment / all	3 / 7		
deaths causally related to treatment / all	0 / 1		
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tendon rupture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thoracic vertebral fracture			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transfusion reaction			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Traumatic haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Upper limb fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound dehiscence			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Acute myocardial infarction			
subjects affected / exposed	9 / 2233 (0.40%)		
occurrences causally related to treatment / all	1 / 9		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	1 / 9		
deaths causally related to treatment / all	0 / 0		
Aortic valve incompetence			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	21 / 2233 (0.94%)		
occurrences causally related to treatment / all	1 / 24		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block first degree			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	16 / 2233 (0.72%)		
occurrences causally related to treatment / all	4 / 16		
deaths causally related to treatment / all	4 / 11		
Cardiac disorder			

subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Cardiac failure			
subjects affected / exposed	43 / 2233 (1.93%)		
occurrences causally related to treatment / all	7 / 45		
deaths causally related to treatment / all	0 / 10		
Cardiac failure acute			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Cardiac failure chronic			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	7 / 2233 (0.31%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 1		
Cardiac tamponade			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	9 / 2233 (0.40%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 5		
Cardiogenic shock			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 4		
Cardiopulmonary failure			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Conduction disorder			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Congestive cardiomyopathy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cor pulmonale			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive heart disease			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracardiac thrombus			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Left ventricular dysfunction			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Left ventricular failure			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Left ventricular hypertrophy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mitral valve incompetence			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	1 / 3		
Myocardial ischaemia			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Pericardial haemorrhage			

subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Right ventricular dysfunction				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Right ventricular failure				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stress cardiomyopathy				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	3 / 2233 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Tachyarrhythmia				

subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tricuspid valve incompetence				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular dysfunction				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular hypokinesia				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Basilar artery aneurysm				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Central nervous system haemorrhage				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Central nervous system lesion				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cerebral haemorrhage				

subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cerebral ischaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Coma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cranial nerve paralysis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Drop attacks			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dysarthria			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolic stroke			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Encephalopathy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Extrapyramidal disorder			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Headache			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Hepatic encephalopathy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperaesthesia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydrocephalus			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscle contractions involuntary			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myoclonus			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurological decompensation			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osmotic demyelination syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			

subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Parkinson's disease			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyramidal tract syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Somnolence			

subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Speech disorder				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	11 / 2233 (0.49%)			
occurrences causally related to treatment / all	1 / 12			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	5 / 2233 (0.22%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Agranulocytosis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	94 / 2233 (4.21%)			
occurrences causally related to treatment / all	52 / 104			
deaths causally related to treatment / all	1 / 1			
Autoimmune haemolytic anaemia				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bone marrow oedema				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coagulopathy				

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	4 / 9		
deaths causally related to treatment / all	0 / 0		
Haemolytic anaemia			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Histiocytosis haematophagic			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercoagulation			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 0		
Leukostasis syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphadenopathy			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphocytosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	10 / 2233 (0.45%)		
occurrences causally related to treatment / all	5 / 10		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Polycythaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Splenic haematoma			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Splenic infarction			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Splenomegaly			

subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Spontaneous haematoma			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	24 / 2233 (1.07%)		
occurrences causally related to treatment / all	9 / 24		
deaths causally related to treatment / all	0 / 0		
Thrombocytosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Vertigo			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Corneal oedema			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diplopia			

subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Macular degeneration				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Optic ischaemic neuropathy				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Uveitis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal hernia				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal mass				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	28 / 2233 (1.25%)			
occurrences causally related to treatment / all	3 / 30			
deaths causally related to treatment / all	0 / 0			
Abdominal pain lower				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				

subjects affected / exposed	5 / 2233 (0.22%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Abdominal tenderness				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal wall haematoma				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal fissure				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anal prolapse				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal ulcer				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	14 / 2233 (0.63%)			
occurrences causally related to treatment / all	3 / 14			
deaths causally related to treatment / all	0 / 0			
Barrett's oesophagus				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				

subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	17 / 2233 (0.76%)		
occurrences causally related to treatment / all	1 / 18		
deaths causally related to treatment / all	0 / 0		
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticular perforation			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterovesical fistula			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Faecaloma			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral hernia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Gastric stenosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric varices haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	21 / 2233 (0.94%)		
occurrences causally related to treatment / all	2 / 23		
deaths causally related to treatment / all	0 / 1		
Haematemesis			

subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Inguinal hernia			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia strangulated			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal infarction			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mallory-Weiss syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Melaena			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Mesenteric haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Mesenteric vein thrombosis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Mouth haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Oesophageal haemorrhage			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Oesophageal rupture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Oesophageal varices haemorrhage			
subjects affected / exposed	10 / 2233 (0.45%)		
occurrences causally related to treatment / all	1 / 11		
deaths causally related to treatment / all	0 / 1		
Pancreatitis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peritoneal haemorrhage			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumoperitoneum			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Rectal polyp			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal haematoma			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal stenosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Splenic artery aneurysm			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Tooth loss			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toothache			

subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	5 / 2233 (0.22%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Varices oesophageal				
subjects affected / exposed	5 / 2233 (0.22%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	16 / 2233 (0.72%)			
occurrences causally related to treatment / all	3 / 17			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermal cyst				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatitis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erythema nodosum				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperhidrosis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Panniculitis				

subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pruritus				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Skin lesion				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin mass				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	19 / 2233 (0.85%)			
occurrences causally related to treatment / all	4 / 21			
deaths causally related to treatment / all	0 / 3			
Acute prerenal failure				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anuria				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Calculus bladder				

subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chronic kidney disease			
subjects affected / exposed	6 / 2233 (0.27%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Dysuria			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	6 / 2233 (0.27%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Nephropathy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrotic syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal colic			

subjects affected / exposed	3 / 2233 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	12 / 2233 (0.54%)			
occurrences causally related to treatment / all	2 / 12			
deaths causally related to treatment / all	0 / 1			
Renal impairment				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Renal infarct				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tubulointerstitial nephritis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenal insufficiency				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Arthropathy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	2 / 8		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	11 / 2233 (0.49%)		
occurrences causally related to treatment / all	0 / 12		
deaths causally related to treatment / all	0 / 0		
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Compartment syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Crystal arthropathy			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Flank pain			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gouty arthritis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemarthrosis			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meniscal degeneration			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscle haemorrhage			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscle tightness			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myalgia			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neck pain			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteolysis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Osteoporotic fracture			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue necrosis			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Actinomycosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Aspergillus infection			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacterial infection			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Biliary sepsis			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone tuberculosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	9 / 2233 (0.40%)		
occurrences causally related to treatment / all	0 / 10		
deaths causally related to treatment / all	0 / 0		
Bronchitis bacterial			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopulmonary aspergillosis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Campylobacter infection			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 1		
Cerebral toxoplasmosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Community acquired infection			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Corneal abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Dengue fever			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dermo-hypodermitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Device related sepsis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Endocarditis			

subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Enterococcal infection			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enterococcal sepsis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epididymitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Escherichia infection			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			
subjects affected / exposed	6 / 2233 (0.27%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gangrene			

subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	11 / 2233 (0.49%)		
occurrences causally related to treatment / all	5 / 12		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis norovirus			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis salmonella			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Genital herpes			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
H1N1 influenza			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic echinococciasis			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis B			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis E			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis infectious			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes simplex			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes simplex pneumonia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
Herpes zoster infection neurological			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			

subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	1 / 1		
Klebsiella infection			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Localised infection			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Lung abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	11 / 2233 (0.49%)		
occurrences causally related to treatment / all	2 / 11		
deaths causally related to treatment / all	0 / 0		
Lymph node tuberculosis			

subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Meningitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Mycobacterial infection			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neurocryptococcosis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pelvic inflammatory disease			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Perirectal abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Peritoneal tuberculosis			

subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	4 / 2233 (0.18%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Peritonitis bacterial				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Pharyngitis				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumococcal infection				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii infection				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	123 / 2233 (5.51%)			
occurrences causally related to treatment / all	24 / 140			
deaths causally related to treatment / all	1 / 16			
Pneumonia bacterial				
subjects affected / exposed	2 / 2233 (0.09%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pseudomonal sepsis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psoas abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Pulmonary tuberculosis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pulpitis dental			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Q fever			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	19 / 2233 (0.85%)		
occurrences causally related to treatment / all	2 / 20		
deaths causally related to treatment / all	1 / 2		
Sepsis			
subjects affected / exposed	31 / 2233 (1.39%)		
occurrences causally related to treatment / all	5 / 33		
deaths causally related to treatment / all	0 / 10		
Septic shock			
subjects affected / exposed	21 / 2233 (0.94%)		
occurrences causally related to treatment / all	3 / 21		
deaths causally related to treatment / all	2 / 12		
Sinusitis			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	6 / 2233 (0.27%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 1		
Soft tissue infection			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal sepsis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tooth abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheobronchitis			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			
subjects affected / exposed	5 / 2233 (0.22%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Tubo-ovarian abscess			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			

subjects affected / exposed	3 / 2233 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	23 / 2233 (1.03%)			
occurrences causally related to treatment / all	3 / 25			
deaths causally related to treatment / all	0 / 1			
Urinary tract infection bacterial				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	8 / 2233 (0.36%)			
occurrences causally related to treatment / all	1 / 8			
deaths causally related to treatment / all	0 / 0			
Vestibular neuronitis				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Cachexia				
subjects affected / exposed	3 / 2233 (0.13%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Decreased appetite				
subjects affected / exposed	1 / 2233 (0.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	3 / 9		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fluid retention			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	8 / 2233 (0.36%)		
occurrences causally related to treatment / all	2 / 8		
deaths causally related to treatment / all	0 / 0		
Hyperlactacidaemia			

subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperuricaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	2 / 2233 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypovolaemia			
subjects affected / exposed	1 / 2233 (0.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			

subjects affected / exposed	3 / 2233 (0.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	4 / 2233 (0.18%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	INC424		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2008 / 2233 (89.92%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	134 / 2233 (6.00%)		
occurrences (all)	166		
Platelet count decreased			
subjects affected / exposed	198 / 2233 (8.87%)		
occurrences (all)	323		
Weight increased			
subjects affected / exposed	140 / 2233 (6.27%)		
occurrences (all)	152		
Nervous system disorders			
Headache			
subjects affected / exposed	191 / 2233 (8.55%)		
occurrences (all)	231		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1300 / 2233 (58.22%)		
occurrences (all)	2207		
Neutropenia			
subjects affected / exposed	146 / 2233 (6.54%)		
occurrences (all)	219		
Thrombocytopenia			

subjects affected / exposed	990 / 2233 (44.33%)		
occurrences (all)	1775		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	331 / 2233 (14.82%)		
occurrences (all)	423		
Fatigue			
subjects affected / exposed	215 / 2233 (9.63%)		
occurrences (all)	253		
Oedema peripheral			
subjects affected / exposed	182 / 2233 (8.15%)		
occurrences (all)	210		
Pyrexia			
subjects affected / exposed	310 / 2233 (13.88%)		
occurrences (all)	422		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	149 / 2233 (6.67%)		
occurrences (all)	174		
Constipation			
subjects affected / exposed	121 / 2233 (5.42%)		
occurrences (all)	134		
Diarrhoea			
subjects affected / exposed	267 / 2233 (11.96%)		
occurrences (all)	358		
Nausea			
subjects affected / exposed	128 / 2233 (5.73%)		
occurrences (all)	147		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	186 / 2233 (8.33%)		
occurrences (all)	206		
Dyspnoea			

subjects affected / exposed	155 / 2233 (6.94%)		
occurrences (all)	172		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	131 / 2233 (5.87%)		
occurrences (all)	149		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	176 / 2233 (7.88%)		
occurrences (all)	218		
Back pain			
subjects affected / exposed	115 / 2233 (5.15%)		
occurrences (all)	125		
Pain in extremity			
subjects affected / exposed	147 / 2233 (6.58%)		
occurrences (all)	168		
Infections and infestations			
Herpes zoster			
subjects affected / exposed	112 / 2233 (5.02%)		
occurrences (all)	125		
Nasopharyngitis			
subjects affected / exposed	115 / 2233 (5.15%)		
occurrences (all)	140		
Urinary tract infection			
subjects affected / exposed	114 / 2233 (5.11%)		
occurrences (all)	162		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 August 2012	1. To re-evaluate the inclusion and exclusion criteria to the study 2. Increase the enrollment sample size from 950 to 1600 patients plus a 20% attrition rate 3. Addition of interim analyses
11 September 2013	1. Addition of inclusion criteria for patients having a 50000 to 75000/ µL baseline platelet count if all other inclusion/exclusion criteria are met, and addition of dosing instructions for those patients for an initial dose of 5 mg po bid. 2. The sample size is to be increased up to a maximum of 2484. 3. Enrollment to the study will complete when the maximum number of patients has been enrolled or December 31, 2014, whichever comes first. 4. The decision regarding end of treatment will now include physician decision. 5. Data analysis will no longer be performed annually, but may be performed if needed to fulfill regulatory request or publication purpose. 6. Where Country-specific local Health Authority approval is in process, drug supply is updated to take into account that drug may be supplied centrally, or locally if deemed necessary after local Health Authority approval have been granted. 7. Statistical analysis reflecting updates in estimated end of enrollment and end of treatment, with inclusion of patients with baseline platelet count of 50000 to 75000/µL in the pool of patients with low platelet counts. 8. Update AE definition and processing. 9. Update reference list.
17 December 2013	1. Addition of inclusion criteria to allow fedratinib pretreated patients to be included in the trial as long as clinical, laboratory and image assessments are properly documented. 2. Update of visit schedule and assessments.
21 March 2016	The primary purpose of the amendment was to align this protocol with the latest modified Novartis standard language for clinical study protocols: *Updated highly effective contraception method The “contraception use” wording has been updated to provide clarification and implement latest available guidelines as to highly effective contraception. Since all patients are enrolled, the clarification does not apply per se to exclusion criteria but may be used as needed for female of childbearing potential currently enrolled in the trial, *Updates to concomitant therapy and prohibited concomitant therapy Clarifications to concomitant therapy and prohibited concomitant therapy is also updated in appendix. *Additional changes: Reticulocytes count and coagulation parameters determination may or may not be part of the standard evaluation performed in clinical practice at different health care centers. As this study aims to resemble the use of ruxolitinib in patients with myelofibrosis in the clinical practice setting, we will allow optional collection and results reporting in the CRF when collected and deemed clinically relevant on a patient basis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported