Clinical trial results:
A Multicenter, Open Label Study to Assess the Safety and Efficacy of Risankizumab for Maintenance in Moderate to Severe Plaque Type Psoriasis

Summary

EudraCT number	2016-003046-87
Trial protocol	AT SE BE DE FI CZ PL PT ES FR
Global end of trial date	30 November 2023

Results information

Result version number	v1 (current)
This version publication date	06 December 2024
First version publication date	06 December 2024

Trial information

Trial identification

Sponsor protocol code	M15-997

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03047395
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of Study M15-997 is to investigate long-term safety and tolerability of risankizumab in subjects with psoriasis who have completed one of the preceding Phase 2/3 studies.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 61
Country: Number of subjects enrolled	Austria: 13
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Canada: 432
Country: Number of subjects enrolled	Czechia: 38
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 256
Country: Number of subjects enrolled	Japan: 217
Country: Number of subjects enrolled	Korea, Republic of: 94
Country: Number of subjects enrolled	Mexico: 39
Country: Number of subjects enrolled	Poland: 86
Country: Number of subjects enrolled	Portugal: 19
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	Taiwan: 51
Country: Number of subjects enrolled	United States: 815
Worldwide total number of subjects	2170
EEA total number of subjects	461

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)	1922
From 65 to 84 years	247
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants from Studies M16-008, M16-010, M15-995, M16-178, M16-009, M15-992, and M16-004 entered this open-label extension (OLE) study from 232 sites across 17 countries (Australia, Austria, Belgium, Canada, Czech Republic, Finland, France, Germany, Japan, Mexico, Poland, Portugal, Republic of Korea, Spain, Sweden, Taiwan, US).

Pre-assignment

Screening details:

Participants were eligible for study enrollment if he/she met all inclusion criteria and none of the exclusion criteria at the Baseline visit.

Period 1

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

Arms

Arm title	Risankizumab 150 mg

Arm description:

Risankizumab 150 mg administered by subcutaneous injection every 12 weeks.

Arm type	Experimental
Investigational medicinal product name	Risankizumab
Investigational medicinal product code	ABBV-066
Other name	Skyrizi, BI 655066
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Risankizumab 150 mg administered by subcutaneous injection every 12 weeks.

Number of subjects in period 1	Risankizumab 150 mg
Started	2170
Completed	1601
Not completed	569
Consent withdrawn by subject	155
Other, not specified	117
Adverse event	142
COVID-19 logistical restrictions	9
Lost to follow-up	144
COVID-19 infection	2

Baseline characteristics

Reporting groups	
Reporting group title	Risankizumab 150 mg
Reporting group description:	
Risankizumab 150 mg administered by subcutaneous injection every 12 weeks.	

Reporting group values	Risankizumab 150 mg	Total	
Number of subjects	2170	2170	
Age categorical Units: Subjects			
< 40 years	658	658	
40 - < 65 years	1264	1264	
>= 65 years	248	248	
Gender categorical Units: Subjects			
Female	634	634	
Male	1536	1536	
Ethnicity Units: Subjects			
Hispanic or Latino	257	257	
Not Hispanic or Latino	1913	1913	
Race Units: Subjects			
American Indian or Alaska Native	15	15	
Asian	466	466	
Native Hawaiian or Other Pacific Islander	9	9	
Black or African American	50	50	
White	1622	1622	
More than one race	8	8	

End points

End points reporting groups

Reporting group title	Risankizumab 150 mg

Reporting group description:

Risankizumab 150 mg administered by subcutaneous injection every 12 weeks.

Primary: Number of Participants With Serious Adverse Events or Non-Serious Adverse Events

End point title	Number of Participants With Serious Adverse Events or Non-Serious Adverse Events[1]

End point description:

An adverse event is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed the relationship of each event to the use of study drug as either probably related, possibly related, probably not related or not related. A serious adverse event is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above.

End point type	Primary

End point timeframe:

Median follow-up time of 1905 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics are presented per protocol.

End point values	Risankizumab 150 mg			
Subject group type	Reporting group			
Number of subjects analysed	2170			
Units: participants				
Serious Adverse Events	435			
Non-serious Adverse Events	1215			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Median follow-up time of 1905 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0
Reporting groups	
Reporting group title	Risankizumab 150mg
Reporting group description: Risankizumab 150 mg administered by subcutaneous injection every 12 weeks	

Serious adverse events	Risankizumab 150mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	435 / 2170 (20.05%)		
number of deaths (all causes)	28		
number of deaths resulting from adverse events	28		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
COLORECTAL ADENOCARCINOMA			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
ANAL CANCER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
BASAL CELL CARCINOMA			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
BILE DUCT CANCER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

BLADDER CANCER			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
BLADDER TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BORDERLINE MUCINOUS TUMOUR OF OVARY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BRAIN NEOPLASM MALIGNANT			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COLON CANCER STAGE 0			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
COLON CANCER METASTATIC			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CLEAR CELL RENAL CELL CARCINOMA			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
CHRONIC LYMPHOCYTIC LEUKAEMIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

CHROMOPHOBE RENAL CELL CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
BREAST CANCER STAGE II			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BREAST CANCER RECURRENT			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
BREAST CANCER			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
ADENOCARCINOMA OF COLON			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
INVASIVE LOBULAR BREAST CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LARYNGEAL CANCER STAGE II			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LARYNGEAL SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

LIPOSARCOMA METASTATIC			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
LUNG ADENOCARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LUNG CANCER METASTATIC			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COLORECTAL ADENOMA			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
COLORECTAL CANCER			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ENDOMETRIAL CANCER STAGE II			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTRIC CANCER			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
GERM CELL CANCER METASTATIC			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GLIOBLASTOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HAEMANGIOMA OF LIVER			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HEPATIC CANCER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INVASIVE BREAST CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
INVASIVE DUCTAL BREAST CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
MALIGNANT MELANOMA			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
SARCOMA UTERUS			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MENINGIOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
METASTATIC SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PANCREATIC CARCINOMA			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
PANCREATIC CARCINOMA STAGE IV			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PAPILLARY THYROID CANCER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PENILE SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PLASMA CELL MYELOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PROSTATE CANCER			

subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
PROSTATE CANCER METASTATIC			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PROSTATE CANCER STAGE IV			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RECTAL ADENOCARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RECTAL CANCER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL CANCER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL CELL CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
MALIGNANT MELANOMA IN SITU			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
UTERINE CANCER			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SUPERFICIAL SPREADING MELANOMA STAGE I			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SQUAMOUS CELL CARCINOMA OF THE TONGUE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
SCHWANNOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
UTERINE LEIOMYOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

UTERINE MYOMA EXPULSION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRIPLE NEGATIVE BREAST CANCER				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
HYPERTENSIVE URGENCY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERTENSION				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
EMBOLISM ARTERIAL				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
AORTIC ANEURYSM				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
AORTIC STENOSIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ARTERIOSCLEROSIS				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
DEEP VEIN THROMBOSIS				

subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
VARICOSE VEIN				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PELVIC VENOUS THROMBOSIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VASCULAR STENOSIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
ABDOMINOPLASTY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ABORTION INDUCED				
subjects affected / exposed	4 / 2170 (0.18%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
ECLAMPSIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

ABORTION SPONTANEOUS				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
SURGICAL FAILURE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DEATH				
subjects affected / exposed	6 / 2170 (0.28%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 6			
MULTIPLE ORGAN DYSFUNCTION SYNDROME				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
NON-CARDIAC CHEST PAIN				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OEDEMA PERIPHERAL				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PAIN				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SUDDEN CARDIAC DEATH				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			

SUDDEN DEATH			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
VASCULAR STENT STENOSIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
LOSS OF PERSONAL INDEPENDENCE IN DAILY ACTIVITIES			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
BALANOPOSTHITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BREAST ENLARGEMENT			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CYSTOCELE			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ENDOMETRIAL DISORDER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ENDOMETRIOSIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PROSTATITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
PNEUMOTHORAX			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
ASTHMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			

subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
COUGH				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DYSPNOEA EXERTIONAL				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NASAL SEPTUM DEVIATION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONITIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY DISTRESS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PULMONARY EMBOLISM				
subjects affected / exposed	6 / 2170 (0.28%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY FAILURE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
COMPLETED SUICIDE				

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
CATATONIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
BIPOLAR DISORDER				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ANXIETY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ANOREXIA NERVOSA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ALCOHOL WITHDRAWAL SYNDROME				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ALCOHOL ABUSE				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
CONFUSIONAL STATE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DEPRESSED MOOD				

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DEPRESSION				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
POST-TRAUMATIC AMNESTIC DISORDER				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POST-TRAUMATIC STRESS DISORDER				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SCHIZOPHRENIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SOMATIC SYMPTOM DISORDER				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SUICIDE ATTEMPT				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
AUTOIMMUNE HEPATITIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHOLECYSTITIS				

subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
CHOLECYSTITIS ACUTE				
subjects affected / exposed	4 / 2170 (0.18%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 0			
CHOLELITHIASIS				
subjects affected / exposed	6 / 2170 (0.28%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
CIRRHOSIS ALCOHOLIC				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
GALLBLADDER POLYP				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HEPATIC CIRRHOSIS				
subjects affected / exposed	4 / 2170 (0.18%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
HEPATITIS ALCOHOLIC				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ALCOHOLIC LIVER DISEASE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
BLOOD TRIGLYCERIDES INCREASED				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
CARTILAGE INJURY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ACETABULUM FRACTURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ALCOHOL POISONING			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
ANKLE FRACTURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COLON INJURY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LIMB INJURY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CONTUSION			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CRANIOCEREBRAL INJURY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CRANIOFACIAL FRACTURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FALL			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
FEMUR FRACTURE			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
FIBULA FRACTURE			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HAND FRACTURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEAD INJURY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HIP FRACTURE			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HUMERUS FRACTURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTENTIONAL OVERDOSE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
JOINT DISLOCATION			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
LIGAMENT INJURY			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
LIGAMENT RUPTURE			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
CONCUSSION			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
LIMB TRAUMATIC AMPUTATION			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LOWER LIMB FRACTURE			

subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LUMBAR VERTEBRAL FRACTURE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
MENISCUS INJURY				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
MULTIPLE INJURIES				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NAIL INJURY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PATELLA FRACTURE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POST PROCEDURAL COMPLICATION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POST PROCEDURAL HAEMATOMA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POST PROCEDURAL SWELLING				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RADIUS FRACTURE			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
RIB FRACTURE			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
SKIN ABRASION			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TENDON DISLOCATION			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
TENDON INJURY			

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
UPPER LIMB FRACTURE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ULNA FRACTURE				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
TOXICITY TO VARIOUS AGENTS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TIBIA FRACTURE				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
THERMAL BURN				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TENDON RUPTURE				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
WRIST FRACTURE				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
ATRIAL SEPTAL DEFECT				

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CONGENITAL CYSTIC KIDNEY DISEASE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERTROPHIC CARDIOMYOPATHY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
AORTIC VALVE INCOMPETENCE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ACUTE MYOCARDIAL INFARCTION				
subjects affected / exposed	13 / 2170 (0.60%)			
occurrences causally related to treatment / all	2 / 13			
deaths causally related to treatment / all	0 / 0			
ANGINA PECTORIS				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ANGINA UNSTABLE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ACUTE CORONARY SYNDROME				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ARRHYTHMIA				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CORONARY ARTERY OCCLUSION			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIAL FIBRILLATION			
subjects affected / exposed	9 / 2170 (0.41%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
ATRIAL FLUTTER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIAL TACHYCARDIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIOVENTRICULAR BLOCK SECOND DEGREE			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
BIFASCICULAR BLOCK			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BRADYCARDIA			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC ARREST			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	5 / 2170 (0.23%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	1 / 1		
CARDIAC VENTRICULAR THROMBOSIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
CARDIOMYOPATHY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIOVASCULAR DISORDER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
CORONARY ARTERY DISEASE			
subjects affected / exposed	9 / 2170 (0.41%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
ARTERIOSCLEROSIS CORONARY ARTERY			

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DRESSLER'S SYNDROME				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERICARDIAL EFFUSION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PERICARDITIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PRINZMETAL ANGINA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SINUS NODE DYSFUNCTION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SUPRAVENTRICULAR TACHYCARDIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VENTRICULAR EXTRASYSTOLES				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VENTRICULAR FIBRILLATION				

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
MYOCARDIAL INFARCTION				
subjects affected / exposed	9 / 2170 (0.41%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 2			
Nervous system disorders				
CEREBROVASCULAR ACCIDENT				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
BELL'S PALSY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CAROTID ARTERY STENOSIS				
subjects affected / exposed	4 / 2170 (0.18%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
CEREBRAL HAEMATOMA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CEREBRAL HAEMORRHAGE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CEREBRAL INFARCTION				
subjects affected / exposed	5 / 2170 (0.23%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
ISCHAEMIC STROKE				

subjects affected / exposed	5 / 2170 (0.23%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
HYPOAESTHESIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEMIPARESIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEADACHE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HAEMORRHAGIC STROKE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
EPILEPSY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DIZZINESS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DEMENTIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
METABOLIC ENCEPHALOPATHY			

subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
SEIZURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RUPTURED CEREBRAL ANEURYSM			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PROGRESSIVE SUPRANUCLEAR PALSY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PRESYNCOPE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PARTIAL SEIZURES			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PARAESTHESIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NEURALGIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MULTIPLE SCLEROSIS			

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SENSORY DISTURBANCE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SUBARACHNOID HAEMORRHAGE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SYNCOPE				
subjects affected / exposed	7 / 2170 (0.32%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
THALAMIC INFARCTION				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
TOXIC ENCEPHALOPATHY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRANSIENT ISCHAEMIC ATTACK				
subjects affected / exposed	5 / 2170 (0.23%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
VERTEBROBASILAR INSUFFICIENCY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STATUS EPILEPTICUS				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
FEBRILE NEUTROPENIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HAEMOLYSIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PANCYTOPENIA			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
SUDDEN HEARING LOSS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VERTIGO			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VERTIGO POSITIONAL			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

BLINDNESS UNILATERAL				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CATARACT				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
EPIRETINAL MEMBRANE				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
MACULAR HOLE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
GASTRIC ULCER				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ABDOMINAL HERNIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ABDOMINAL INCARCERATED HERNIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ASCITES				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHRONIC GASTRITIS				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COLITIS ISCHAEMIC			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DUODENAL ULCER			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DYSPEPSIA			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
GASTRITIS EROSIVE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
HAEMATEMESIS			

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMATOCHEZIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HAEMORRHOIDS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INCARCERATED INGUINAL HERNIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INCARCERATED UMBILICAL HERNIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INGUINAL HERNIA				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
INTESTINAL ISCHAEMIA				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
INTESTINAL OBSTRUCTION				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LARGE INTESTINE PERFORATION				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LARGE INTESTINE POLYP			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OESOPHAGEAL STENOSIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
OESOPHAGITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
GASTRITIS			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RECTAL STENOSIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RETROPERITONEAL MASS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SMALL INTESTINAL OBSTRUCTION			

subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
TOOTH DISORDER				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
UMBILICAL HERNIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
UPPER GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VOMITING				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RECTAL HAEMORRHAGE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
ANGIOEDEMA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ECZEMA				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LICHEN PLANUS				

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PRECANCEROUS SKIN LESION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STEVENS-JOHNSON SYNDROME				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
PYELOCALIECTASIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RENAL ARTERY STENOSIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RENAL COLIC				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ACUTE KIDNEY INJURY				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
CALCULUS URINARY				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
CYSTITIS INTERSTITIAL				

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYDRONEPHROSIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NEPHROLITHIASIS				
subjects affected / exposed	8 / 2170 (0.37%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 0			
PELVI-URETERIC OBSTRUCTION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RENAL CYST				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
GOITRE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
GRAVES' DISEASE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
THYROTOXIC CRISIS				

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERTHYROIDISM				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
BACK PAIN				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ARTHRALGIA				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
PAIN IN EXTREMITY				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OSTEONECROSIS				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
OSTEOARTHRITIS				
subjects affected / exposed	17 / 2170 (0.78%)			
occurrences causally related to treatment / all	0 / 20			
deaths causally related to treatment / all	0 / 0			
LUMBAR SPINAL STENOSIS				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LOOSE BODY IN JOINT				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	6 / 2170 (0.28%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
FOOT DEFORMITY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CERVICAL SPINAL STENOSIS			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
PSORIATIC ARTHROPATHY			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
TENDINOUS CONTRACTURE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SYNOVITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SYNOVIAL CYST			

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SPONDYLOLISTHESIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SPINAL STENOSIS				
subjects affected / exposed	4 / 2170 (0.18%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
SPINAL LIGAMENT OSSIFICATION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ROTATOR CUFF SYNDROME				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
TENOSYNOVITIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
BRONCHIOLITIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
ABSCESS JAW				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ABSCESS LIMB				

subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
APPENDICITIS			
subjects affected / exposed	6 / 2170 (0.28%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 0		
ARTHRITIS BACTERIAL			
subjects affected / exposed	3 / 2170 (0.14%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
BURSITIS INFECTIVE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
INTERVERTEBRAL DISCITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CELLULITIS OF MALE EXTERNAL GENITAL ORGAN			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CHRONIC TONSILLITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			

subjects affected / exposed	13 / 2170 (0.60%)		
occurrences causally related to treatment / all	3 / 14		
deaths causally related to treatment / all	1 / 5		
COVID-19 PNEUMONIA			
subjects affected / exposed	7 / 2170 (0.32%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 2		
DIVERTICULITIS			
subjects affected / exposed	6 / 2170 (0.28%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
EPIDIDYMITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
ERYSIPELAS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FALLOPIAN TUBE ABSCESS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FOURNIER'S GANGRENE			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GAS GANGRENE			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HERPES ZOSTER			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
INFECTIVE GLOSSITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CELLULITIS			
subjects affected / exposed	5 / 2170 (0.23%)		
occurrences causally related to treatment / all	3 / 6		
deaths causally related to treatment / all	0 / 0		
LARGE INTESTINE INFECTION			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PSOAS ABSCESS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
MENINGITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NEUROSYPHILIS			

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
ORCHITIS			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
OSTEOMYELITIS			
subjects affected / exposed	4 / 2170 (0.18%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
PERICORONITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PERIRECTAL ABSCESS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PERITONITIS			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
PERITONSILLAR ABSCESS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA			
subjects affected / exposed	7 / 2170 (0.32%)		
occurrences causally related to treatment / all	3 / 7		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA ASPIRATION			

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
PNEUMONIA BACTERIAL				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA VIRAL				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POST PROCEDURAL INFECTION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POSTOPERATIVE ABSCESS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PSEUDOMONAL SEPSIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
MEDIASTINAL ABSCESS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PYELONEPHRITIS				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
RENAL ABSCESS				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SCROTAL ABSCESS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
SEPSIS			
subjects affected / exposed	6 / 2170 (0.28%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
SEPTIC SHOCK			
subjects affected / exposed	2 / 2170 (0.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
TONSILLITIS			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
UROSEPSIS			

subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VESTIBULAR NEURONITIS				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PYELONEPHRITIS ACUTE				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
DEHYDRATION				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DIABETES MELLITUS				
subjects affected / exposed	3 / 2170 (0.14%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
DIABETIC KETOACIDOSIS				
subjects affected / exposed	2 / 2170 (0.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
ELECTROLYTE IMBALANCE				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERGLYCAEMIA				
subjects affected / exposed	1 / 2170 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPOKALAEMIA				

subjects affected / exposed	1 / 2170 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OBESITY			
subjects affected / exposed	4 / 2170 (0.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Risankizumab 150mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1215 / 2170 (55.99%)		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	227 / 2170 (10.46%)		
occurrences (all)	245		
Nervous system disorders			
HEADACHE			
subjects affected / exposed	134 / 2170 (6.18%)		
occurrences (all)	211		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	124 / 2170 (5.71%)		
occurrences (all)	142		
ARTHRALGIA			
subjects affected / exposed	217 / 2170 (10.00%)		
occurrences (all)	267		
Infections and infestations			
COVID-19			
subjects affected / exposed	360 / 2170 (16.59%)		
occurrences (all)	384		
NASOPHARYNGITIS			

subjects affected / exposed	480 / 2170 (22.12%)			
occurrences (all)	833			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	312 / 2170 (14.38%)			
occurrences (all)	467			

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2016	The purpose of this amendment is to: ● Specify primary objective of the study is to investigate long term safety and tolerability of risankizumab in subjects with psoriasis. ● Specify secondary objective of the study is to investigate long term efficacy of risankizumab in subjects with psoriasis. ● Add Inclusion Criterion 2 from Section 1.1, Synopsis, to Section 5.2.1, Inclusion Criteria. ● Clarify Section 5.2.4, Contraception Recommendations and Pregnancy Testing, contraception language regarding methotrexate (MTX). ● Add definition of the PASI50 endpoint to Section 5.3.3.2, Additional Variables. ● Add the 25th and 75th percentiles to Section 8.1.4, Statistical Analysis of Efficacy. ● Add the 95% Confidence Intervals to Section 8.1.4, Statistical Analysis of Efficacy. ● Add a detailed description of the pharmacokinetic analysis. ● Add details on Use of Information (Section 12.0, Use of Information). ● Add details on Data Quality Assurance (Section 11.0, Data Quality Assurance).
06 June 2017	The purpose of this amendment is to: ● Add Study M16-178 as additional preceding study that could enroll subjects in Study M15-997. ● Increase expected number of subjects enrolled to 2000. ● Add the possibility to have qualified and delegated site staff members to perform the efficacy assessments. ● Add "arm" as additional possible injection site. ● Update the relationship to study drug definitions. ● Add information on Interim Database Lock in Q4 2017. ● Correct typographical and grammatical errors throughout the document.
10 January 2018	The purpose of this amendment is to: ● Add Study 1311.13 as additional preceding study that could enroll subjects in Study M15-997. • Update the exception for prohibited topical treatments for psoriasis or any other skin condition.
21 June 2018	The purpose of this amendment is to: ● Extend the period between the last administered dose of risankizumab and the End of Observation Visit from 16 to 20 weeks. ● Update the number of subjects to be enrolled to approximately 2200. ● Revise inclusion and exclusion criteria to require that women of childbearing potential use contraception throughout the study, including 20 weeks after the last dose of study drug, and exclude subjects who are pregnant, breastfeeding or considering becoming pregnant throughout the study, including 20 weeks after the last dose of study drug. ● Add the establishment of an independent external Anaphylaxis Adjudication Committee (AAC). ● Add request to draw additional blood samples in case of a suspected systemic post-dose hypersensitivity reaction and conduct additional blood tests in case of a systemic hypersensitivity reaction. ● Update the treatment-emergent AE definition to include events until 20 weeks (140 days) after the last risankizumab injection. ● Decrease the pharmacokinetic (PK) and anti-drug antibody (ADA) sample collection. ● Correct typographical and grammatical errors and make some small clarifying changes throughout the document.

24 September 2019	The purpose of this amendment is to: ● Update the Sponsor/Emergency contact/Primary Therapeutic Area Medical Director ● Extend the study duration from 156 weeks to 252 weeks with study visits every 24 weeks after Week 156. ● Allow self-administration of risankizumab at home at Weeks 168, 192, 216 and 240 and add corresponding requirements for this. ● Update the Introduction and the Benefits and Risks section of the protocol to match the latest Investigator Brochure. ● Remove the need to consult with the AbbVie TAMD for use of lower potency topical steroids and define the limited period of time for use being approximately 6 weeks. ● Add clearer guidance on when study drug administration may resume after being postponed for a serious infection. ● Remove drug storage temperature excursion requirements. ● Remove the necessity to retain empty IP boxes and sharps containers at site until the AbbVie monitor is on site to confirm the medication. ● Update the definitions of analysis populations. ● Remove short-term efficacy summary. ● Correct typographical and grammatical errors and make some small clarifying changes throughout the document.
26 November 2019	The purpose of this amendment is to: • Remove the sentence "In the event that a suspected anaphylactic reaction occurs while the subject is not on site at the study clinic, the treating facility should be advised to perform serum tryptase and histamine to help better understand and characterize the diagnosis." from the section Monitoring for Hypersensitivity Reaction.
17 November 2020	The purpose of this amendment is to: Incorporate necessary protocol modifications due to the COVID-19 pandemic as follows: ● Section 1.3 – added COVID-19 Specific Abbreviations ● Section 3.2 – included information on the re-evaluation of the benefit and risk to subjects participating in the study. ● Section 5.1 – added that study visits may be impacted due to the COVID-19 pandemic. ● Section 5.3.1.1 – updated to include details on how to perform specific activities/procedures that may be impacted by changes in global/local regulations due to the pandemic ● Section 5.4.1 – included guidance on interruption or discontinuation of study drug due to COVID-19 infection ● Section 5.5.4 – included instructions on possible Direct-to patient study drug shipment ● Section 6.1.5 – added information on reporting requirements in the eCRF in the event of COVID-19 related missed/virtual visits, study drug interruptions or discontinuation, or adverse events ● Section 7.0 – clarified that protocol deviations may include modifications due to COVID-19 ● Section 10.2 – noted that supplemental study case report form should be completed in the event of COVID-19 related missed/virtual visits, study drug discontinuations, or adverse events and that remote monitoring may be employed as needed. ● State that monitoring by the independent Data Monitoring Committee will no longer be in effect for this open-label study. ● Clarify which cardiovascular adverse events will be formally adjudicated. ● Clarify the discontinuation criteria. ● Clarify that following discontinuation of study drug subjects can be treated in accordance with the Investigator's best clinical judgement. ● Update the Sponsor/Emergency contact/Primary Therapeutic Area Medical Director.

18 October 2021	The purpose of this amendment is to: ● Throughout the protocol, remove the requirement for the physical exam, clinical laboratory samples and efficacy assessments PASI, sPGA, NAPSI, PPASI, PSSI, and the DLQI at the End of Observation (EOO) visit and change the EOO visit from an in-person visit to a phone visit. ● Change the End of Observation visit requirement to perform an ECG, TB testing and additional clinical laboratory testing to the EOT visit in Appendix C ("Study Activities Flow Chart"). ● Clarify the analysis of the immunogenicity samples in Section 5.3.2.4 ("Measurement Methods"). ● Add INR test to be performed if ALT or AST > 3 x ULN to Table 1 Clinical Laboratory Test in Section 5.3.1.1 ("Study Procedures"). ●Update the definition of hepatic injury to include marked peak aminotransferase elevations ≥ 8-fold ULN, instead of ≥ 10-fold ULN in Section 6.1.1.3 ("Adverse Events of Special Interests"). ● Clarify in Section 6.1.1.3 Adverse Events of Special Interests, that the supplemental hepatic eCRFs have to be completed for any hepatic related AE leading to discontinuation or interruption of study drug or any hepatic related SAE, not meeting the hepatic injury definition. ● Add language to address potential use of SARS-CoV-2 vaccines to Section 5.2.3 ("Prior and Concomitant Therapy") and Section 6.1.5 ("Adverse Event Reporting"). ● Update the Sponsor/Emergency contact/Primary Therapeutic Area Medical Director and Alternate Contact for Protocol Deviations in Section 1.0 ("Title Page"), Section 6.1.5 ("Adverse Event Reporting") and Section 7.0 ("Protocol Deviations").

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported