Clinical trial results:
Phase III trial of combined immunochemotherapy with Fludarabine, Cyclophosphamide and Rituximab (FCR) versus Bendamustine and Rituximab (BR) in patients with previously untreated chronic lymphocytic leukemia

Summary

EudraCT number	2007-007587-21
Trial protocol	DE AT DK CZ
Global end of trial date	01 January 2018

Results information

Result version number	v1 (current)
This version publication date	21 August 2020
First version publication date	21 August 2020

Trial information

Trial identification

Sponsor protocol code	CLL10

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00769522
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	German CLL Study Group, University Hospital Cologne
Sponsor organisation address	Gleuelerstr. 176-178, Cologne, Germany, 50935
Public contact	Information Desk, German CLL Study Group, +49 22147888198, cll-studie@uk-koeln.de
Scientific contact	Information Desk, German CLL Study Group, +49 22147888198, cll-studie@uk-koeln.de

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	12 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 December 2017
Global end of trial reached?	Yes
Global end of trial date	01 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to demonstrate that BR has a non-inferior therapeutic efficacy compared with FCR, but a better safety profile causing less myelosuppression, infections and secondary neoplasias.

Protection of trial subjects:

For a prevention of an anaphylactic reaction and a cytokine release Syndrome patients should be pretreated with antihistamines, Paracetamol/Acetaminophen and Prednisolon.
In case of a leukocytopenia CTC grade 3 or 4 with a Duration of >7 days, phophylaxis of pneumocystis carinii-pneumonia is recommended. Other routine measures such as antibiotic, antimycotic or viostatic prophylaxis as well as the use of growth factors should be given if clinically indicated.

Background therapy:

Chemoimmunotherapy with fludarabine, cyclophosphamide and rituximab (FCR) is the Standard therapy for physically fit patients with acvanced chronic lymphocytic leukaemia and Background therapy in the CLL10-trial.
Following the results of a Phase 2 study by the MD Anderson Cancer Center and a Phase 3 Study by the German CLL-Study Group, the CLL8 study, FCR has become the Standard front-line therapy for physically fit patients with chronic lymphocytic leukemia. However this Regimen ist associated with substantial toxic effects, most importantly severe haematotoxicity in 56% of patients and severe infections in 25% of patients during treatment. A Long-term follow-up of patients treated with FCR showed prolonged neutropenia in 17-35% and an elevated risk of secondary neoplasia.

Evidence for comparator:

Chemoimmunotherapy with bendamustine and rituximab (BR) is the comparator. The combination of the akylating Agent bendamustine and rituximab has shown promising results in a Phase 2 study in front-line therapy of chronic lymphocytic leukaemia with Overall responses in 103 of 117 patients and complete responses in 27 of 117 patients. Event-free survival of 34 months and low incidence of severe neutropenia (20%) and infections (8%) led to the hypothesis that the treatment with BR might be similarly effective but less toxic compared with the Standard treatment FCR.

Actual start date of recruitment	02 October 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 10
Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	Denmark: 24
Country: Number of subjects enrolled	Germany: 487
Country: Number of subjects enrolled	Switzerland: 36

Worldwide total number of subjects	561
EEA total number of subjects	525

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)	353
From 65 to 84 years	208
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

564 patients were enrolled between 10/2008 and 04/2012. The patients were randomly assigned to FCR (284) and BR (280) .
561 patients were allocated to treatment because 3 patients dropped off during the randomisation process. 282 patients were allocated to FCR and 279 patients were allocated to BR (baseline values).

Pre-assignment

Screening details:

688 treatment-naïve patients diagnosed with CLL were registered for central screening . The central screening was performed by the GCLLSG central study office in Cologne, Germany and included immunophenotyping, FISH, evaluation of the comorbidity and renal function. 127 patients were not eligible for participation.

Pre-assignment period milestones

Number of subjects started	688[1]
Number of subjects completed	561

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 127

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: All patients who meet the eligibility criteria for study entry can be enrolled into the trial. To verify the eligibility of patients, a patient screening by a medical review of the pretherapeutic staging as well as a central immunophenotyping for confirmation of the diagnosis and FISH analysis to exclude patients with a 17p deletion or mutation will be performed before randomization.
688 patients started pre-assignment period. 127 patients were assessed as Screening failures. 561 completed.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Fludarabine/Cyclophosphamide/Rituximab

Arm description:

Chemoimmunotherapy with fludarabine, cyclophosphamide and rituximab.

Arm type	Standard
Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Cycle 1-6 on days 1-3: 25mg/m2

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Cytoxan
Pharmaceutical forms	Powder for solution for infusion

Routes of administration	Intravenous use
Dosage and administration details: 250 mg/m2 cycle 1-6 on days 1, 2, 3.	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	Rituxan, Truxima
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Cycle 1: 375 mg/ m2 i.v. on day 0 Cycles 2-6: 500 mg/ m2 i.v. on day 1 (before FC)	

Arm title	Bendamustine/Rituximab
Arm description: Chemoimmunotherapy with bendamustine and rituximab	
Arm type	Active comparator
Investigational medicinal product name	Bendamustine
Investigational medicinal product code	
Other name	Ribomustin, Treanda
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 90 mg/m² course 1-6, days 1 and 2	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	Rituxan, Truxima
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Cycle1: 375mg/m2 i.v. on day 0 cycles 2-6: 500 mg/m2 i.v. on day 1 (before FC)	

Number of subjects in period 1	Fludarabine/Cyclophosphamide/Rituximab	Bendamustine/Rituximab
Started	282	279
treatment allocation	282	279
treatment	282	279
follow-up	282	279
Completed	199	224
Not completed	83	55
Adverse event, serious fatal	3	1
withdrawal of consent before start of treatment	3	1
Adverse event, non-fatal	65	38
various reasons	10	14
Lack of efficacy	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Fludarabine/Cyclophosphamide/Rituximab
Reporting group description: Chemoimmunotherapy with fludarabine, cyclophosphamide and rituximab.	
Reporting group title	Bendamustine/Rituximab
Reporting group description: Chemoimmunotherapy with bendamustine and rituximab	

Reporting group values	Fludarabine/Cyclophosphamide/Rituximab	Bendamustine/Rituximab	Total
Number of subjects	282	279	561
Age categorical			
Median Age 60.5 years for FCR and 62.0 years for BR.			
Units: Subjects			
Adults (18-64 years)	187	166	353
65 years and over	95	113	208
Age continuous			
Units: years			
median	60.5	62	
inter-quartile range (Q1-Q3)	55 to 67	54 to 69	-
Gender categorical			
Units: Subjects			
Female	81	72	153
Male	201	207	408

Subject analysis sets	
Subject analysis set title	CLL10 Clinical Study Report
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat population (ITT) included all randomized subjects. 561 Patients (282 patients in the FCR arm and 279 patients in the BR arm) were assessed for progression free survival PFS (primary endpoint). PFS was measured from the date of randomization to the date of first documented disease progression (as defined by the IWCLL 2008 response criteria) or death by any cause, whichever occurred first . Following secondary endpoints were assessed:
duration of Remission, event free survival (EFS), overall survival (OS), MRD, complete response rates and partial remission rates, response rates and survival times in biological subgroups, rates of toxicities and quality of life.

Reporting group values	CLL10 Clinical Study Report		
Number of subjects	561		
Age categorical			
Median Age 60.5 years for FCR and 62.0 years for BR.			
Units: Subjects			
Adults (18-64 years)	353		
65 years and over	208		

Age continuous Units: years			
median	61		
inter-quartile range (Q1-Q3)	54.5 to 68.0		
Gender categorical Units: Subjects			
Female	153		
Male	408		

End points

End points reporting groups

Reporting group title	Fludarabine/Cyclophosphamide/Rituximab
Reporting group description: Chemoimmunotherapy with fludarabine, cyclophosphamide and rituximab.	
Reporting group title	Bendamustine/Rituximab
Reporting group description: Chemoimmunotherapy with bendamustine and rituximab	
Subject analysis set title	CLL10 Clinical Study Report
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The intent-to-treat population (ITT) included all randomized subjects. 561 Patients (282 patients in the FCR arm and 279 patients in the BR arm) were assessed for progression free survival PFS (primary endpoint). PFS was measured from the date of randomization to the date of first documented disease progression (as defined by the IWCLL 2008 response criteria) or death by any cause, whichever occurred first . Following secondary endpoints were assessed:
duration of Remission, event free survival (EFS), overall survival (OS), MRD, complete response rates and partial remission rates, response rates and survival times in biological subgroups, rates of toxicities and quality of life.

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Progression free survival will be calculated as the time between date of randomization and date of progression or death of any cause.

End point type	Primary

End point timeframe:

The progression free survival (PFS) rate after 24 months

End point values	Fludarabine/Cyclophosphamide/Rituximab	Bendamustine/Rituximab	CLL10 Clinical Study Report	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	282	279	561	
Units: PFS rates at 24 months				
number (not applicable)	84.3	77.8	81.0	

Statistical analyses

Statistical analysis title	Statistical plan for primary endpoint

Statistical analysis description:

Progression-free survival (PFS) is defined as the time from randomization to disease progression or death from any cause. These will be counted as events for PFS. Patients who have neither progressed nor died will be censored.
A Cox proportional hazard model will be applied on progression-free survival time including the variables for study medication and the stratification parameters as covariates. If the upper limit of the 90.4%-confidence interval of the hazard-ratio of BR compared to FCR is

Comparison groups	Fludarabine/Cyclophosphamide/Rituximab v

	Bendamustine/Rituximab
Number of subjects included in analysis	561
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.643
Confidence interval	
level	90.4 %
sides	1-sided
upper limit	2.064

Notes:

[1] - The significance level of the study is 5% (one-sided, with one interim analysis and one final analysis using the method of O'Brien and Fleming to allocate the global 5% significance level to the 2 analyses), the significance level of the final analysis is accordingly 4.8%. The power is 80%.
The CLL 10 protocol is a non-inferiority trial. The expected PFS 2 years after start of FCR therapy is 75% which translates to an exponential parameter of 0.1438.
[2] - A p value < 0.001 and an upper limit of the 90.4% confidence interval is greater than 1.388. Thus, the null hypothesis for the corresponding non-inferiority hypothesis cannot be rejected according to the protocol.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Chemoimmunotherapy BR

Reporting group description: -

Reporting group title	Chemoimmunotherapy FCR

Reporting group description: -

Serious adverse events	Chemoimmunotherapy BR	Chemoimmunotherapy FCR	
Total subjects affected by serious adverse events			
subjects affected / exposed	135 / 278 (48.56%)	155 / 279 (55.56%)	
number of deaths (all causes)	78	69	
number of deaths resulting from adverse events	14	20	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia	Additional description: Acute myeloid leukaemia		
subjects affected / exposed	1 / 278 (0.36%)	4 / 279 (1.43%)	
occurrences causally related to treatment / all	0 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	3 / 3	
Adenocarcinoma	Additional description: Adenocarcinoma		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Basal cell carcinoma	Additional description: Basal cell carcinoma		
subjects affected / exposed	1 / 278 (0.36%)	4 / 279 (1.43%)	
occurrences causally related to treatment / all	1 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer	Additional description: Bladder cancer		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm	Additional description: Bladder neoplasm		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer	Additional description: Breast cancer		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma	Additional description: Bronchial carcinoma		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Breast cancer female	Additional description: Breast cancer female		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell sarcoma of the kidney	Additional description: Clear cell sarcoma of the kidney		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic	Additional description: Colon cancer metastatic		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer	Additional description: Colorectal cancer		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Glioblastoma	Additional description: Glioblastoma		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma	Additional description: Malignant melanoma		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant neoplasm of unknown primary site	Additional description: Malignant neoplasm of unknown primary site		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelodysplastic syndrome	Additional description: Myelodysplastic syndrome		
subjects affected / exposed	1 / 278 (0.36%)	4 / 279 (1.43%)	
occurrences causally related to treatment / all	0 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic neoplasm	Additional description: Metastatic neoplasm		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal adenocarcinoma	Additional description: Oesophageal adenocarcinoma		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer	Additional description: Prostate cancer		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer	Additional description: Rectal cancer		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Refractory anaemia with an excess of blasts	Additional description: Refractory anaemia with an excess of blasts		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer	Additional description: Skin cancer		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma of skin	Additional description: Squamous cell carcinoma of skin		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer	Additional description: Thyroid cancer		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma	Additional description: Transitional cell carcinoma		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm	Additional description: Aortic aneurysm		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension	Additional description: Hypertension		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication	Additional description: Intermittent claudication		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis	Additional description: Peripheral artery stenosis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis	Additional description: Thrombophlebitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hernia repair	Additional description: Hernia repair		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty	Additional description: Hip arthroplasty		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip surgery	Additional description: Hip surgery		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc operation	Additional description: Intervertebral disc operation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee operation	Additional description: Knee operation		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung lobectomy	Additional description: Lung lobectomy		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus operation	Additional description: Meniscus operation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagectomy	Additional description: Oesophagectomy		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Osteotomy	Additional description: Osteotomy		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile prosthesis insertion	Additional description: Penile prosthesis insertion		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatectomy	Additional description: Prostatectomy		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal operation	Additional description: Spinal operation		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal laminectomy	Additional description: Spinal laminectomy		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal decompression	Additional description: Spinal decompression		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroidectomy	Additional description: Thyroidectomy		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death	Additional description: Death		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	17 / 278 (6.12%)	15 / 279 (5.38%)	
occurrences causally related to treatment / all	14 / 17	17 / 19	
deaths causally related to treatment / all	0 / 0	1 / 1	
Immune system disorders			
Anaphylactic reaction	Additional description: Anaphylactic reaction		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock	Additional description: Anaphylactic shock		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytokine release syndrome	Additional description: Cytokine release syndrome		
subjects affected / exposed	4 / 278 (1.44%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Drug hypersensitivity	Additional description: Drug hypersensitivity		
subjects affected / exposed	3 / 278 (1.08%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	7 / 278 (2.52%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	7 / 7	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serum sickness	Additional description: Serum sickness		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia	Additional description: Benign prostatic hyperplasia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus prostatic	Additional description: Calculus prostatic		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis	Additional description: Prostatitis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration	Additional description: Aspiration		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma	Additional description: Asthma		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial haemorrhage	Additional description: Bronchial haemorrhage		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chylothorax	Additional description: Chylothorax		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups	Additional description: Hiccups		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration	Additional description: Lung infiltration		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis	Additional description: Pneumonitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax	Additional description: Pneumothorax		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	3 / 278 (1.08%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary sarcoidosis	Additional description: Pulmonary sarcoidosis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder	Additional description: Respiratory disorder		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcoholism	Additional description: Alcoholism		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute psychosis	Additional description: Acute psychosis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Arthroscopy	Additional description: Arthroscopy		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biopsy adrenal gland	Additional description: Biopsy adrenal gland		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood sodium decreased	Additional description: Blood sodium decreased		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigation	Additional description: Investigation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count	Additional description: Neutrophil count		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Allergic transfusion reaction	Additional description: Allergic transfusion reaction		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture	Additional description: Ankle fracture		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial injury	Additional description: Arterial injury		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture	Additional description: Cervical vertebral fracture		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall	Additional description: Fall		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture	Additional description: Femoral neck fracture		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture	Additional description: Foot fracture		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	3 / 278 (1.08%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria	Additional description: Post procedural haematuria		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident	Additional description: Road traffic accident		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture	Additional description: Tendon rupture		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction	Additional description: Transfusion reaction		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome	Additional description: Acute coronary syndrome		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction	Additional description: Acute myocardial infarction		
subjects affected / exposed	3 / 278 (1.08%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arrhythmia	Additional description: Arrhythmia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	4 / 278 (1.44%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter	Additional description: Atrial flutter		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia	Additional description: Atrial tachycardia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia	Additional description: Bradyarrhythmia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure	Additional description: Cardiac failure		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery dilatation	Additional description: Coronary artery dilatation		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease	Additional description: Coronary artery disease		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	3 / 278 (1.08%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial ischaemia	Additional description: Myocardial ischaemia		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion	Additional description: Pericardial effusion		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia	Additional description: Tachyarrhythmia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebellar ischaemia	Additional description: Cerebellar ischaemia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia	Additional description: Cerebral ischaemia		

subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic hyperosmolar coma	Additional description: Diabetic hyperosmolar coma		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness	Additional description: Dizziness		
subjects affected / exposed	0 / 278 (0.00%)	3 / 279 (1.08%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Horner's syndrome	Additional description: Horner's syndrome		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukoencephalopathy	Additional description: Leukoencephalopathy		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope	Additional description: Syncope		
subjects affected / exposed	3 / 278 (1.08%)	3 / 279 (1.08%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack	Additional description: Transient ischaemic attack		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		

subjects affected / exposed	0 / 278 (0.00%)	6 / 279 (2.15%)	
occurrences causally related to treatment / all	0 / 0	6 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	13 / 278 (4.68%)	18 / 279 (6.45%)	
occurrences causally related to treatment / all	11 / 13	18 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia	Additional description: Febrile bone marrow aplasia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis	Additional description: Haemolysis		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia	Additional description: Haemolytic anaemia		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	1 / 278 (0.36%)	4 / 279 (1.43%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia	Additional description: Pancytopenia		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet disorder	Additional description: Platelet disorder		

subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional	Additional description: Vertigo positional		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment	Additional description: Retinal detachment		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen	Additional description: Acute abdomen		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphthous stomatitis	Additional description: Aphthous stomatitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	0 / 278 (0.00%)	3 / 279 (1.08%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diverticulum	Additional description: Diverticulum		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastritis erosive	Additional description: Gastritis erosive		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Inguinal hernia	Additional description: Inguinal hernia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Large intestine perforation	Additional description: Large intestine perforation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutropenic colitis	Additional description: Neutropenic colitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

Pancreatitis	Additional description: Pancreatitis

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	2 / 278 (0.72%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	2 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis	Additional description: Cholelithiasis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiolitis	Additional description: Cholangiolitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic	Additional description: Hepatitis toxic		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity	Additional description: Hepatotoxicity		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis allergic	Additional description: Dermatitis allergic		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema	Additional description: Eczema		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema	Additional description: Erythema		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkeratosis	Additional description: Hyperkeratosis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukoplakia	Additional description: Leukoplakia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash	Additional description: Rash		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash generalised	Additional description: Rash generalised		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic epidermal necrolysis	Additional description: Toxic epidermal necrolysis		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Bladder malposition acquired	Additional description: Bladder malposition acquired		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus ureteric	Additional description: Calculus ureteric		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis	Additional description: Nephrolithiasis		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis	Additional description: Arthritis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthrofibrosis	Additional description: Arthrofibrosis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain	Additional description: Back pain		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis	Additional description: Osteoarthritis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess of salivary gland	Additional description: Abscess of salivary gland		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess	Additional description: Anal abscess		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis	Additional description: Bacterial sepsis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bacterial infection	Additional description: Bacterial infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	3 / 278 (1.08%)	6 / 279 (2.15%)	
occurrences causally related to treatment / all	0 / 4	3 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchopneumonia	Additional description: Bronchopneumonia		
subjects affected / exposed	3 / 278 (1.08%)	3 / 279 (1.08%)	
occurrences causally related to treatment / all	1 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis	Additional description: Bronchopulmonary aspergillosis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic sinusitis	Additional description: Chronic sinusitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile sepsis	Additional description: Clostridium difficile sepsis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis	Additional description: Cystitis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis	Additional description: Diverticulitis		

subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences causally related to treatment / all	2 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas	Additional description: Erysipelas		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection	Additional description: Escherichia urinary tract infection		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection	Additional description: Febrile infection		
subjects affected / exposed	3 / 278 (1.08%)	6 / 279 (2.15%)	
occurrences causally related to treatment / all	3 / 3	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial	Additional description: Gastroenteritis clostridial		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection	Additional description: Gastrointestinal infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus	Additional description: Gastroenteritis norovirus		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital herpes	Additional description: Genital herpes		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza	Additional description: H1N1 influenza		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B	Additional description: Hepatitis B		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	2 / 278 (0.72%)	9 / 279 (3.23%)	
occurrences causally related to treatment / all	0 / 2	3 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus	Additional description: Herpes zoster oticus		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza	Additional description: Influenza		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection	Additional description: Infection		
subjects affected / exposed	3 / 278 (1.08%)	4 / 279 (1.43%)	
occurrences causally related to treatment / all	5 / 6	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection	Additional description: Lung infection		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection	Additional description: Neutropenic infection		

subjects affected / exposed	4 / 278 (1.44%)	3 / 279 (1.08%)	
occurrences causally related to treatment / all	4 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis	Additional description: Neutropenic sepsis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis	Additional description: Oesophageal candidiasis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis	Additional description: Pharyngitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural infection	Additional description: Pleural infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia	Additional description: Pneumocystis jirovecii pneumonia		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial	Additional description: Pneumonia bacterial		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	21 / 278 (7.55%)	25 / 279 (8.96%)	
occurrences causally related to treatment / all	13 / 22	16 / 31	
deaths causally related to treatment / all	2 / 2	1 / 2	
Pneumonia haemophilus	Additional description: Pneumonia haemophilus		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal	Additional description: Pneumonia mycoplasmal		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal	Additional description: Pneumonia pneumococcal		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral	Additional description: Pneumonia viral		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural sepsis	Additional description: Post procedural sepsis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Progressive multifocal leukoencephalopathy	Additional description: Progressive multifocal leukoencephalopathy		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary sepsis	Additional description: Pulmonary sepsis		
subjects affected / exposed	1 / 278 (0.36%)	3 / 279 (1.08%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 2	
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection	Additional description: Rhinovirus infection		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess	Additional description: Scrotal abscess		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis	Additional description: Sepsis		
subjects affected / exposed	3 / 278 (1.08%)	5 / 279 (1.79%)	
occurrences causally related to treatment / all	1 / 3	3 / 5	
deaths causally related to treatment / all	1 / 2	2 / 2	
Sinobronchitis	Additional description: Sinobronchitis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis	Additional description: Sinusitis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection	Additional description: Soft tissue infection		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis	Additional description: Tonsillitis		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	2 / 278 (0.72%)	7 / 279 (2.51%)	
occurrences causally related to treatment / all	2 / 2	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		

subjects affected / exposed	3 / 278 (1.08%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis	Additional description: Lactic acidosis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Chemoimmunotherapy BR	Chemoimmunotherapy FCR	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	248 / 278 (89.21%)	271 / 279 (97.13%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma	Additional description: Basal cell carcinoma		
subjects affected / exposed	2 / 278 (0.72%)	2 / 279 (0.72%)	
occurrences (all)	2	3	
Breast cancer	Additional description: Breast cancer		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Colon adenoma	Additional description: Colon adenoma		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Histiocytosis	Additional description: Histiocytosis		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Oesophageal adenocarcinoma	Additional description: Oesophageal adenocarcinoma		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	2	
Seborrhoeic keratosis	Additional description: Seborrhoeic keratosis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Skin cancer	Additional description: Skin cancer		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Skin papilloma	Additional description: Skin papilloma		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences (all)	2	1	
Squamous cell carcinoma of skin	Additional description: Squamous cell carcinoma of skin		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Thyroid cancer	Additional description: Thyroid cancer		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Haemorrhage	Additional description: Haemorrhage		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Hot flush	Additional description: Hot flush		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Hypertension	Additional description: Hypertension		
subjects affected / exposed	4 / 278 (1.44%)	2 / 279 (0.72%)	
occurrences (all)	4	3	
Hypotension	Additional description: Hypotension		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	2	0	

Labile blood pressure	Additional description: Labile blood pressure		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Peripheral ischaemia	Additional description: Peripheral ischaemia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Phlebitis	Additional description: Phlebitis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Post thrombotic syndrome	Additional description: Post thrombotic syndrome		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	3	
Thrombosis	Additional description: Thrombosis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Thrombophlebitis	Additional description: Thrombophlebitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Varicose vein	Additional description: Varicose vein		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Venous thrombosis limb	Additional description: Venous thrombosis limb		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Catheter management	Additional description: Catheter management		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Cervical conisation	Additional description: Cervical conisation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Haemorrhoid operation	Additional description: Haemorrhoid operation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Hysterectomy	Additional description: Hysterectomy		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Immunoglobulin therapy	Additional description: Immunoglobulin therapy		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Papilloma excision	Additional description: Papilloma excision		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Shoulder operation	Additional description: Shoulder operation		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Skin neoplasm excision	Additional description: Skin neoplasm excision		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Chest pain	Additional description: Chest pain		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Chills	Additional description: Chills		
subjects affected / exposed	4 / 278 (1.44%)	1 / 279 (0.36%)	
occurrences (all)	4	1	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	6 / 278 (2.16%)	8 / 279 (2.87%)	
occurrences (all)	8	16	
Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Inflammation	Additional description: Inflammation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Influenza like illness	Additional description: Influenza like illness		

subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences (all)	2	5	
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	3 / 278 (1.08%)	2 / 279 (0.72%)	
occurrences (all)	3	2	
Oedema	Additional description: Oedema		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Pain	Additional description: Pain		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	38 / 278 (13.67%)	42 / 279 (15.05%)	
occurrences (all)	45	57	
Ulcer	Additional description: Ulcer		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Immune system disorders			
Anaphylactic reaction	Additional description: Anaphylactic reaction		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Cytokine release syndrome	Additional description: Cytokine release syndrome		
subjects affected / exposed	3 / 278 (1.08%)	1 / 279 (0.36%)	
occurrences (all)	3	1	
Drug hypersensitivity	Additional description: Drug hypersensitivity		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Hypersensitivity	Additional description: Hypersensitivity		
subjects affected / exposed	17 / 278 (6.12%)	10 / 279 (3.58%)	
occurrences (all)	19	10	
Hypogammaglobulinaemia	Additional description: Hypogammaglobulinaemia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	4	0	

Type IV hypersensitivity reaction	Additional description: Type IV hypersensitivity reaction		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Benign prostatic hyperplasia	Additional description: Benign prostatic hyperplasia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Erectile dysfunction	Additional description: Erectile dysfunction		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	7	0	
Prostatitis	Additional description: Prostatitis		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Vaginal discharge	Additional description: Vaginal discharge		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Vulvovaginal dryness	Additional description: Vulvovaginal dryness		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis	Additional description: Allergic bronchitis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Bronchitis chronic	Additional description: Bronchitis chronic		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences (all)	2	1	
Bronchospasm	Additional description: Bronchospasm		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Chronic obstructive pulmonary disease	Additional description: Chronic obstructive pulmonary disease		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	2	

Chylothorax	Additional description: Chylothorax		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Cough	Additional description: Cough		
subjects affected / exposed	10 / 278 (3.60%)	18 / 279 (6.45%)	
occurrences (all)	11	25	
Cough decreased	Additional description: Cough decreased		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	3 / 278 (1.08%)	4 / 279 (1.43%)	
occurrences (all)	11	7	
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences (all)	2	1	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Productive cough	Additional description: Productive cough		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Rhinitis allergic	Additional description: Rhinitis allergic		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Rhinitis atrophic	Additional description: Rhinitis atrophic		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	3	

Psychiatric disorders			
Depression	Additional description: Depression		
subjects affected / exposed	4 / 278 (1.44%)	2 / 279 (0.72%)	
occurrences (all)	6	2	
Insomnia	Additional description: Insomnia		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	4	2	
Schizophrenia	Additional description: Schizophrenia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase	Additional description: Alanine aminotransferase		
subjects affected / exposed	0 / 278 (0.00%)	3 / 279 (1.08%)	
occurrences (all)	0	5	
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	0 / 278 (0.00%)	3 / 279 (1.08%)	
occurrences (all)	0	4	
Aspartate aminotransferase	Additional description: Aspartate aminotransferase		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	4	
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Blood creatinine	Additional description: Blood creatinine		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin	Additional description: Blood bilirubin		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased	Additional description: Blood lactate dehydrogenase increased		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Body temperature increased	Additional description: Body temperature increased		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Blood potassium decreased	Additional description: Blood potassium decreased		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	2	
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
CD4 lymphocytes	Additional description: CD4 lymphocytes		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
CD4 lymphocytes decreased	Additional description: CD4 lymphocytes decreased		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	9	
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 278 (0.00%)	3 / 279 (1.08%)	
occurrences (all)	0	4	
Gamma-glutamyltransferase	Additional description: Gamma-glutamyltransferase		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	11	
Haemoglobin	Additional description: Haemoglobin		
subjects affected / exposed	9 / 278 (3.24%)	10 / 279 (3.58%)	
occurrences (all)	17	35	
Granulocytes abnormal	Additional description: Granulocytes abnormal		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	5	
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	3	
Hepatitis B antibody positive	Additional description: Hepatitis B antibody positive		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	

Hepatic enzyme increased	Additional description: Hepatic enzyme increased		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	2	
Immunoglobulins decreased	Additional description: Immunoglobulins decreased		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	3	1	
Intraocular pressure increased	Additional description: Intraocular pressure increased		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Lipase	Additional description: Lipase		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Neutrophil count	Additional description: Neutrophil count		
subjects affected / exposed	20 / 278 (7.19%)	33 / 279 (11.83%)	
occurrences (all)	41	89	
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	1 / 278 (0.36%)	3 / 279 (1.08%)	
occurrences (all)	2	3	
Platelet count	Additional description: Platelet count		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Prothrombin time shortened	Additional description: Prothrombin time shortened		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Transaminases increased	Additional description: Transaminases increased		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
White blood cell count	Additional description: White blood cell count		
subjects affected / exposed	15 / 278 (5.40%)	26 / 279 (9.32%)	
occurrences (all)	38	92	
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	

Injury, poisoning and procedural complications			
Arterial injury	Additional description: Arterial injury		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	8	
Foot fracture	Additional description: Foot fracture		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences (all)	2	3	
Meniscus injury	Additional description: Meniscus injury		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences (all)	2	1	
Postoperative fever	Additional description: Postoperative fever		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Skull fracture	Additional description: Skull fracture		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Wound	Additional description: Wound		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Cardiac disorders			
Angina pectoris	Additional description: Angina pectoris		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Arrhythmia	Additional description: Arrhythmia		
subjects affected / exposed	3 / 278 (1.08%)	1 / 279 (0.36%)	
occurrences (all)	3	1	
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Cardiac failure	Additional description: Cardiac failure		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Myocardial ischaemia	Additional description: Myocardial ischaemia		

subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Tachyarrhythmia	Additional description: Tachyarrhythmia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Nervous system disorders			
Carotid artery stenosis	Additional description: Carotid artery stenosis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Carpal tunnel syndrome	Additional description: Carpal tunnel syndrome		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	4	
Cervicogenic headache	Additional description: Cervicogenic headache		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Depressed level of consciousness	Additional description: Depressed level of consciousness		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Dizziness	Additional description: Dizziness		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Dystonia	Additional description: Dystonia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Headache	Additional description: Headache		
subjects affected / exposed	3 / 278 (1.08%)	0 / 279 (0.00%)	
occurrences (all)	3	0	
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Monoparesis	Additional description: Monoparesis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	

Migraine with aura	Additional description: Migraine with aura		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Memory impairment	Additional description: Memory impairment		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Neuralgia	Additional description: Neuralgia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Paresis cranial nerve	Additional description: Paresis cranial nerve		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Parkinson's disease	Additional description: Parkinson's disease		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Polyneuropathy	Additional description: Polyneuropathy		
subjects affected / exposed	3 / 278 (1.08%)	2 / 279 (0.72%)	
occurrences (all)	10	2	
Post herpetic neuralgia	Additional description: Post herpetic neuralgia		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	5	
Restless legs syndrome	Additional description: Restless legs syndrome		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Syncope	Additional description: Syncope		
subjects affected / exposed	3 / 278 (1.08%)	0 / 279 (0.00%)	
occurrences (all)	3	0	
Transient ischaemic attack	Additional description: Transient ischaemic attack		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	

Blood and lymphatic system disorders			
Anaemia vitamin B12 deficiency	Additional description: Anaemia vitamin B12 deficiency		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Anaemia folate deficiency	Additional description: Anaemia folate deficiency		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Anaemia	Additional description: Anaemia		
subjects affected / exposed	18 / 278 (6.47%)	26 / 279 (9.32%)	
occurrences (all)	30	39	
Autoimmune haemolytic anaemia	Additional description: Autoimmune haemolytic anaemia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	4 / 278 (1.44%)	4 / 279 (1.43%)	
occurrences (all)	6	4	
Granulocytopenia	Additional description: Granulocytopenia		
subjects affected / exposed	3 / 278 (1.08%)	3 / 279 (1.08%)	
occurrences (all)	4	3	
Haemolytic anaemia	Additional description: Haemolytic anaemia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Haemolysis	Additional description: Haemolysis		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	2	1	
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	127 / 278 (45.68%)	208 / 279 (74.55%)	
occurrences (all)	321	818	
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	153 / 278 (55.04%)	216 / 279 (77.42%)	
occurrences (all)	369	802	
Pancytopenia	Additional description: Pancytopenia		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	3	
Platelet disorder	Additional description: Platelet disorder		

subjects affected / exposed	5 / 278 (1.80%)	8 / 279 (2.87%)	
occurrences (all)	6	22	
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	45 / 278 (16.19%)	61 / 279 (21.86%)	
occurrences (all)	86	138	
Ear and labyrinth disorders			
Deafness	Additional description: Deafness		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Hearing impaired	Additional description: Hearing impaired		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Tinnitus	Additional description: Tinnitus		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Vestibular disorder	Additional description: Vestibular disorder		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	2	
Vertigo	Additional description: Vertigo		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Age-related macular degeneration	Additional description: Age-related macular degeneration		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Glaucoma	Additional description: Glaucoma		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Visual impairment	Additional description: Visual impairment		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			

Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 278 (0.36%)	3 / 279 (1.08%)	
occurrences (all)	1	3	
Anal fissure	Additional description: Anal fissure		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Anal prolapse	Additional description: Anal prolapse		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Anal ulcer	Additional description: Anal ulcer		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Aphthous stomatitis	Additional description: Aphthous stomatitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Chronic gastritis	Additional description: Chronic gastritis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Colitis	Additional description: Colitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences (all)	1	2	
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 278 (0.72%)	4 / 279 (1.43%)	
occurrences (all)	2	6	
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	

Enteritis	Additional description: Enteritis		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences (all)	1	2	
Enterocolitis	Additional description: Enterocolitis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Gastric ulcer	Additional description: Gastric ulcer		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Gastritis	Additional description: Gastritis		
subjects affected / exposed	3 / 278 (1.08%)	0 / 279 (0.00%)	
occurrences (all)	5	0	
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	3 / 278 (1.08%)	0 / 279 (0.00%)	
occurrences (all)	4	0	
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Ileus	Additional description: Ileus		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Inguinal hernia	Additional description: Inguinal hernia		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Nausea	Additional description: Nausea		
subjects affected / exposed	7 / 278 (2.52%)	5 / 279 (1.79%)	
occurrences (all)	7	8	
Oral mucosal discolouration	Additional description: Oral mucosal discolouration		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Periodontal inflammation	Additional description: Periodontal inflammation		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	0 / 278 (0.00%)	4 / 279 (1.43%)	
occurrences (all)	0	4	

Toothache	Additional description: Toothache		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Tooth loss	Additional description: Tooth loss		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	5 / 278 (1.80%)	4 / 279 (1.43%)	
occurrences (all)	5	6	
Hepatobiliary disorders			
Cholelithiasis	Additional description: Cholelithiasis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Hepatitis alcoholic	Additional description: Hepatitis alcoholic		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	2	
Hyperbilirubinaemia	Additional description: Hyperbilirubinaemia		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Acne	Additional description: Acne		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Actinic keratosis	Additional description: Actinic keratosis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Blister	Additional description: Blister		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Dermatitis allergic	Additional description: Dermatitis allergic		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Dermatitis psoriasiform	Additional description: Dermatitis psoriasiform		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Dry skin	Additional description: Dry skin		

subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Eczema	Additional description: Eczema		
subjects affected / exposed	2 / 278 (0.72%)	2 / 279 (0.72%)	
occurrences (all)	3	2	
Erythema	Additional description: Erythema		
subjects affected / exposed	3 / 278 (1.08%)	5 / 279 (1.79%)	
occurrences (all)	4	10	
Erythema nodosum	Additional description: Erythema nodosum		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Erythema multiforme	Additional description: Erythema multiforme		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	0 / 278 (0.00%)	4 / 279 (1.43%)	
occurrences (all)	0	6	
Hyperkeratosis	Additional description: Hyperkeratosis		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	4	0	
Neurodermatitis	Additional description: Neurodermatitis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	11	
Petechiae	Additional description: Petechiae		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Photosensitivity reaction	Additional description: Photosensitivity reaction		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Pruritus	Additional description: Pruritus		
subjects affected / exposed	11 / 278 (3.96%)	8 / 279 (2.87%)	
occurrences (all)	16	12	
Psoriasis	Additional description: Psoriasis		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Rash	Additional description: Rash		

subjects affected / exposed	16 / 278 (5.76%)	16 / 279 (5.73%)	
occurrences (all)	30	18	
Rash generalised	Additional description: Rash generalised		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	6	
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Rash papular	Additional description: Rash papular		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Skin exfoliation	Additional description: Skin exfoliation		
subjects affected / exposed	5 / 278 (1.80%)	0 / 279 (0.00%)	
occurrences (all)	7	0	
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Skin texture abnormal	Additional description: Skin texture abnormal		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Skin ulcer	Additional description: Skin ulcer		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	4	
Urticaria	Additional description: Urticaria		
subjects affected / exposed	5 / 278 (1.80%)	1 / 279 (0.36%)	
occurrences (all)	7	1	
Renal and urinary disorders			
Cystitis noninfective	Additional description: Cystitis noninfective		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Dysuria	Additional description: Dysuria		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	

Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Renal colic	Additional description: Renal colic		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Renal failure	Additional description: Renal failure		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Stress urinary incontinence	Additional description: Stress urinary incontinence		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Autoimmune thyroiditis	Additional description: Autoimmune thyroiditis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Hyperthyroidism	Additional description: Hyperthyroidism		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	3 / 278 (1.08%)	4 / 279 (1.43%)	
occurrences (all)	6	9	
Arthritis	Additional description: Arthritis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Arthrofibrosis	Additional description: Arthrofibrosis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Back pain	Additional description: Back pain		
subjects affected / exposed	3 / 278 (1.08%)	4 / 279 (1.43%)	
occurrences (all)	6	6	
Intervertebral disc protrusion	Additional description: Intervertebral disc protrusion		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Musculoskeletal pain	Additional description: Musculoskeletal pain		

subjects affected / exposed	3 / 278 (1.08%)	0 / 279 (0.00%)	
occurrences (all)	5	0	
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Neck pain	Additional description: Neck pain		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Osteoarthritis	Additional description: Osteoarthritis		
subjects affected / exposed	3 / 278 (1.08%)	2 / 279 (0.72%)	
occurrences (all)	5	6	
Osteopenia	Additional description: Osteopenia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Osteoporosis	Additional description: Osteoporosis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Periarthritis	Additional description: Periarthritis		
subjects affected / exposed	2 / 278 (0.72%)	0 / 279 (0.00%)	
occurrences (all)	3	0	
Polyarthritis	Additional description: Polyarthritis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	2	0	
Polymyalgia rheumatica	Additional description: Polymyalgia rheumatica		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	3	0	
Rheumatoid arthritis	Additional description: Rheumatoid arthritis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	6	0	
Scoliosis	Additional description: Scoliosis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Rotator cuff syndrome	Additional description: Rotator cuff syndrome		

subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	2	
Seronegative arthritis	Additional description: Seronegative arthritis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	3	0	
Spinal osteoarthritis	Additional description: Spinal osteoarthritis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Abscess	Additional description: Abscess		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Abscess jaw	Additional description: Abscess jaw		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Acute tonsillitis	Additional description: Acute tonsillitis		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Aspergillus infection	Additional description: Aspergillus infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Bacteraemia	Additional description: Bacteraemia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	31 / 278 (11.15%)	30 / 279 (10.75%)	
occurrences (all)	44	47	
Bronchopneumonia	Additional description: Bronchopneumonia		
subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences (all)	2	5	
Campylobacter gastroenteritis	Additional description: Campylobacter gastroenteritis		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Candida infection	Additional description: Candida infection		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences (all)	2	2	

Chronic sinusitis	Additional description: Chronic sinusitis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	3 / 278 (1.08%)	2 / 279 (0.72%)	
occurrences (all)	3	2	
Cytomegalovirus infection	Additional description: Cytomegalovirus infection		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Cystitis	Additional description: Cystitis		
subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences (all)	2	5	
Diverticulitis	Additional description: Diverticulitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Dysentery	Additional description: Dysentery		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Ear infection	Additional description: Ear infection		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Erysipelas	Additional description: Erysipelas		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Erythema migrans	Additional description: Erythema migrans		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Febrile infection	Additional description: Febrile infection		
subjects affected / exposed	7 / 278 (2.52%)	7 / 279 (2.51%)	
occurrences (all)	7	7	
Fungal infection	Additional description: Fungal infection		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Fungal skin infection	Additional description: Fungal skin infection		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences (all)	1	2	

Furuncle	Additional description: Furuncle		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Gastroenteritis	Additional description: Gastroenteritis		
subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences (all)	2	3	
Gastrointestinal infection	Additional description: Gastrointestinal infection		
subjects affected / exposed	3 / 278 (1.08%)	3 / 279 (1.08%)	
occurrences (all)	3	3	
Gastroenteritis norovirus	Additional description: Gastroenteritis norovirus		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Gingivitis	Additional description: Gingivitis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Genital infection fungal	Additional description: Genital infection fungal		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
H1N1 influenza	Additional description: H1N1 influenza		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Hepatitis E	Additional description: Hepatitis E		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Herpes zoster	Additional description: Herpes zoster		
subjects affected / exposed	16 / 278 (5.76%)	31 / 279 (11.11%)	
occurrences (all)	19	34	
Herpes virus infection	Additional description: Herpes virus infection		
subjects affected / exposed	5 / 278 (1.80%)	9 / 279 (3.23%)	
occurrences (all)	6	12	
Herpes simplex	Additional description: Herpes simplex		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Infection susceptibility increased	Additional description: Infection susceptibility increased		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	

Infection	Additional description: Infection		
subjects affected / exposed	18 / 278 (6.47%)	12 / 279 (4.30%)	
occurrences (all)	20	12	
Infected varicose vein	Additional description: Infected varicose vein		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Infected bites	Additional description: Infected bites		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Influenza	Additional description: Influenza		
subjects affected / exposed	10 / 278 (3.60%)	5 / 279 (1.79%)	
occurrences (all)	11	5	
Laryngitis	Additional description: Laryngitis		
subjects affected / exposed	2 / 278 (0.72%)	1 / 279 (0.36%)	
occurrences (all)	2	1	
Laryngitis bacterial	Additional description: Laryngitis bacterial		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Localised infection	Additional description: Localised infection		
subjects affected / exposed	4 / 278 (1.44%)	2 / 279 (0.72%)	
occurrences (all)	4	2	
Lung infection	Additional description: Lung infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Lyme disease	Additional description: Lyme disease		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Mastitis	Additional description: Mastitis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	52 / 278 (18.71%)	52 / 279 (18.64%)	
occurrences (all)	67	72	
Muscle abscess	Additional description: Muscle abscess		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	2	

Oesophageal candidiasis	Additional description: Oesophageal candidiasis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Ophthalmic herpes zoster	Additional description: Ophthalmic herpes zoster		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Oral fungal infection	Additional description: Oral fungal infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Oral infection	Additional description: Oral infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	17 / 278 (6.12%)	17 / 279 (6.09%)	
occurrences (all)	23	19	
Otitis media	Additional description: Otitis media		
subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences (all)	2	3	
Pharyngitis	Additional description: Pharyngitis		
subjects affected / exposed	9 / 278 (3.24%)	5 / 279 (1.79%)	
occurrences (all)	9	5	
Pharyngeal chlamydia infection	Additional description: Pharyngeal chlamydia infection		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Pneumocystis jirovecii pneumonia	Additional description: Pneumocystis jirovecii pneumonia		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	13 / 278 (4.68%)	16 / 279 (5.73%)	
occurrences (all)	17	16	
Postoperative wound infection	Additional description: Postoperative wound infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Pulmonary mycosis	Additional description: Pulmonary mycosis		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	

Pyelonephritis	Additional description: Pyelonephritis		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	6 / 278 (2.16%)	15 / 279 (5.38%)	
occurrences (all)	7	21	
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	5 / 278 (1.80%)	6 / 279 (2.15%)	
occurrences (all)	5	7	
Sinobronchitis	Additional description: Sinobronchitis		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences (all)	1	3	
Sinusitis	Additional description: Sinusitis		
subjects affected / exposed	10 / 278 (3.60%)	19 / 279 (6.81%)	
occurrences (all)	13	28	
Skin bacterial infection	Additional description: Skin bacterial infection		
subjects affected / exposed	1 / 278 (0.36%)	2 / 279 (0.72%)	
occurrences (all)	1	2	
Skin infection	Additional description: Skin infection		
subjects affected / exposed	1 / 278 (0.36%)	3 / 279 (1.08%)	
occurrences (all)	1	3	
Staphylococcal infection	Additional description: Staphylococcal infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Tooth abscess	Additional description: Tooth abscess		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	
Tooth infection	Additional description: Tooth infection		
subjects affected / exposed	2 / 278 (0.72%)	3 / 279 (1.08%)	
occurrences (all)	2	3	
Tonsillitis	Additional description: Tonsillitis		
subjects affected / exposed	3 / 278 (1.08%)	3 / 279 (1.08%)	
occurrences (all)	3	3	
Tracheobronchitis	Additional description: Tracheobronchitis		
subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	2	

Vaginal infection	Additional description: Vaginal infection		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	16 / 278 (5.76%)	12 / 279 (4.30%)	
occurrences (all)	18	23	
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	25 / 278 (8.99%)	50 / 279 (17.92%)	
occurrences (all)	32	75	
Vaccination site infection	Additional description: Vaccination site infection		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Varicella	Additional description: Varicella		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Viral infection	Additional description: Viral infection		
subjects affected / exposed	4 / 278 (1.44%)	5 / 279 (1.79%)	
occurrences (all)	4	5	
Wound infection	Additional description: Wound infection		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	1	
Folate deficiency	Additional description: Folate deficiency		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	6	
Gout	Additional description: Gout		
subjects affected / exposed	1 / 278 (0.36%)	0 / 279 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia	Additional description: Hypercholesterolaemia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Hyperglycaemia	Additional description: Hyperglycaemia		

subjects affected / exposed	0 / 278 (0.00%)	2 / 279 (0.72%)	
occurrences (all)	0	3	
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	1	
Iron overload	Additional description: Iron overload		
subjects affected / exposed	0 / 278 (0.00%)	1 / 279 (0.36%)	
occurrences (all)	0	2	
Vitamin B12 deficiency	Additional description: Vitamin B12 deficiency		
subjects affected / exposed	1 / 278 (0.36%)	1 / 279 (0.36%)	
occurrences (all)	1	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 June 2010	Global Amendment with German Protocol version 3.1 and date 25.06.2010 was submitted separately in each Country.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27216274