Clinical trial results:
A Two-Cohort, Open-Label, Multicenter, Study of Trastuzumab Emtansine (T-DM1) in HER2-Positive Locally Advanced or Metastatic Breast Cancer Patients Who Have Received Prior Anti-HER2 and Chemotherapy-Based Treatment

Summary

EudraCT number	2012-001628-37
Trial protocol	DE BE ES SE GB DK HU PT NO AT FI IT GR IE SI BG NL EE IS SK
Global end of trial date	

Results information

Result version number	v1
This version publication date	14 October 2017
First version publication date	14 October 2017

Trial information

Trial identification

Sponsor protocol code	MO28231

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01702571
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	21 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To gain better understanding of the safety profile of trastuzumab emtansine in this study the safety and tolerability of trastuzumab emtansine was investigated in human epidermal growth factor receptor 2 (HER2)-positive locally advanced breast cancer (LABC) and metastatic breast cancer (mBC) patients who had received prior anti-HER2 and chemotherapy-based treatment.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 515
Country: Number of subjects enrolled	Spain: 182
Country: Number of subjects enrolled	United Kingdom: 164
Country: Number of subjects enrolled	Italy: 153
Country: Number of subjects enrolled	Germany: 120
Country: Number of subjects enrolled	Turkey: 71
Country: Number of subjects enrolled	Poland: 55
Country: Number of subjects enrolled	Netherlands: 54
Country: Number of subjects enrolled	Brazil: 50
Country: Number of subjects enrolled	Canada: 50
Country: Number of subjects enrolled	Mexico: 48
Country: Number of subjects enrolled	Australia: 46
Country: Number of subjects enrolled	Ireland: 45
Country: Number of subjects enrolled	Portugal: 39
Country: Number of subjects enrolled	Belgium: 36
Country: Number of subjects enrolled	Denmark: 34
Country: Number of subjects enrolled	Greece: 31
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	Korea, Republic of: 25
Country: Number of subjects enrolled	Norway: 24
Country: Number of subjects enrolled	Taiwan: 22
Country: Number of subjects enrolled	Austria: 21

Country: Number of subjects enrolled	Bulgaria: 20
Country: Number of subjects enrolled	Finland: 20
Country: Number of subjects enrolled	Panama: 17
Country: Number of subjects enrolled	Slovenia: 17
Country: Number of subjects enrolled	Sweden: 16
Country: Number of subjects enrolled	Slovakia: 15
Country: Number of subjects enrolled	Argentina: 14
Country: Number of subjects enrolled	Peru: 12
Country: Number of subjects enrolled	Venezuela, Bolivarian Republic of: 10
Country: Number of subjects enrolled	Croatia: 8
Country: Number of subjects enrolled	Ecuador: 7
Country: Number of subjects enrolled	Estonia: 7
Country: Number of subjects enrolled	Guatemala: 7
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Iceland: 4
Country: Number of subjects enrolled	Luxembourg: 4
Country: Number of subjects enrolled	United Arab Emirates: 4
Country: Number of subjects enrolled	Dominican Republic: 1
Worldwide total number of subjects	2003
EEA total number of subjects	1614

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)	1630
From 65 to 84 years	369
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

The last subject enrolled into Cohort 1 initiated treatment on October 21, 2014. Enrollment into Cohort 2 (subjects only of Asian race) began around the time of the end of enrollment into Cohort 1. Cohort 2 was still in the clinical phase at the time of this report.

Pre-assignment

Screening details:

Subjects with HER2-positive disease with invasive breast cancer and prior treatment (both chemotherapy, alone or with another agent, and an anti-HER2 agent, alone or with another agent) with disease progression during or after the most recent treatment for LABC/mBC or within 6 months of completing adjuvant therapy were included in the study.

Period 1

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

Arms

Arm title	Trastuzumab Emtansine (All Subjects)

Arm description:

This cohort (Cohort 1) enrolled all subjects with human epidermal growth factor receptor 2 (HER2) positive, unresectable, locally advanced breast cancer (LABC) or metastatic breast cancer (mBC) who had received prior anti-HER2 and chemotherapy treatment and had progressed on or after the most recent treatment for LABC or mBC, or within 6 months of completing adjuvant therapy. Subjects received trastuzumab emtansine every 3 weeks until unacceptable toxicity, withdrawal of consent, or disease progression.

Arm type	Experimental
Investigational medicinal product name	Trastuzumab emtansine
Investigational medicinal product code	
Other name	RO5304020, T-DM1, Kadcyla,
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received trastuzumab emtansine 3.6 milligrams per kilogram (mg/kg) intravenously (IV) on Day 1 of a 3-week cycle every 3 weeks until unacceptable toxicity, withdrawal of consent, or disease progression.

Number of subjects in period 1	Trastuzumab Emtansine (All Subjects)
Started	2003
Completed	494
Not completed	1509
Termination by Sponsor	4
Cumulative Toxicity	1
Withdrew Consent	177
Safety Follow-up Close to Data Cut Off	9

Adverse Event	1
On Study Drug at Last Patient/Last Visit	93
Investigator Decision	5
Serious Adverse Event	1
Upper Gastrointestinal Bleeding	1
Death	1067
Progressive Disease	3
Visit Not Completed	1
Lost to follow-up	144
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Trastuzumab Emtansine (All Subjects)

Reporting group description:

This cohort (Cohort 1) enrolled all subjects with human epidermal growth factor receptor 2 (HER2) positive, unresectable, locally advanced breast cancer (LABC) or metastatic breast cancer (mBC) who had received prior anti-HER2 and chemotherapy treatment and had progressed on or after the most recent treatment for LABC or mBC, or within 6 months of completing adjuvant therapy. Subjects received trastuzumab emtansine every 3 weeks until unacceptable toxicity, withdrawal of consent, or disease progression.

Reporting group values	Trastuzumab Emtansine (All Subjects)	Total	
Number of subjects	2003	2003	
Age categorical Units: Subjects			
Adults (18-64 years)	1630	1630	
From 65-84 years	369	369	
85 years and over	4	4	
Age Continuous Units: years			
arithmetic mean	54.5		
standard deviation	± 11.35	-	
Gender, Male/Female Units: Subjects			
Female	1989	1989	
Male	14	14	

End points

End points reporting groups

Reporting group title	Trastuzumab Emtansine (All Subjects)

Reporting group description:

This cohort (Cohort 1) enrolled all subjects with human epidermal growth factor receptor 2 (HER2) positive, unresectable, locally advanced breast cancer (LABC) or metastatic breast cancer (mBC) who had received prior anti-HER2 and chemotherapy treatment and had progressed on or after the most recent treatment for LABC or mBC, or within 6 months of completing adjuvant therapy. Subjects received trastuzumab emtansine every 3 weeks until unacceptable toxicity, withdrawal of consent, or disease progression.

Primary: Percentage of Subjects with Adverse Events of Primary Interest

End point title	Percentage of Subjects with Adverse Events of Primary

End point description:

The adverse events of primary interest (AEPIs) in this study were defined as the following: adverse events (AEs) Grade >/= 3, specifically, hepatic events, allergic reactions, thrombocytopenia and haemorrhage events, all Grade >/= 3 AEs related to trastuzumab emtansine and pneumonitis events of all grades. The safety population included all subjects who had received at least 1 dose of study medication.

End point type	Primary

End point timeframe:

Baseline up to approximately 47 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were performed as this study has only one arm.

End point values	Trastuzumab Emtansine (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	2002			
Units: percentage of subjects				
number (not applicable)	23.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival According to Response Evaluation for Solid Tumors (RECIST) Version (v) 1.1 As Per Investigator Assessment

End point title	Progression-Free Survival According to Response Evaluation for Solid Tumors (RECIST) Version (v) 1.1 As Per Investigator Assessment

End point description:

Progression free survival is defined as the time (in months) between the date of first dose and the date of disease progression or death from any cause. Progressive disease (PD) is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters on study (including baseline). In addition to the relative increase of 20%, the sum of diameters must also demonstrate an absolute increase of >/= 5 millimeters (mm). Intent to Treat (ITT) population 1

included all subjects enrolled in Cohort 1.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death due to any cause, whichever occurs first (assessed every 12 weeks during treatment period thereafter 28-42 days after the last dose or every 3-6 months up to approximately 47 months)

End point values	Trastuzumab Emtansine (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	2003			
Units: months				
median (confidence interval 95%)	6.9 (6 to 7.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival According to RECIST v 1.1 As Per Investigator Assessment

End point title	Overall Survival According to RECIST v 1.1 As Per Investigator Assessment

End point description:

Overall survival is defined as time to death, which is the time from the date of dosing until the date of death, regardless of the cause of death. ITT population 1 included all subjects enrolled in Cohort 1.

End point type	Secondary

End point timeframe:

Baseline until death (up to approximately 47 months)

End point values	Trastuzumab Emtansine (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	2003			
Units: months				
median (confidence interval 95%)	27.2 (25.5 to 28.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Best Overall Response (Complete Response

[CR] or Partial Response [PR]) According to RECIST v 1.1 As Per Investigator Assessment

End point title	Percentage of Subjects with Best Overall Response (Complete Response [CR] or Partial Response [PR]) According to RECIST v 1.1 As Per Investigator Assessment

End point description:

Best Overall Response reported here is the Best confirmed Overall Response. To be assigned a status of PR or CR, i.e., to be a responder, changes in tumor measurements had to be confirmed by repeat assessments that had to be performed no less than 4 weeks after the criteria for response were first met, i.e., subjects needed to have two consecutive assessments of PR or CR. CR: disappearance of all target lesions. PR: At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters, in the absence of CR. ITT population 1 included all subjects enrolled in Cohort 1. Only subjects with measurable disease were included in the analysis.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death due to any cause, whichever occurs first (assessed every 12 weeks during treatment period thereafter 28-42 days after the last dose or every 3-6 months up to approximately 47 months)

End point values	Trastuzumab Emtansine (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	1613			
Units: percentage of subjects				
number (not applicable)	29.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Clinical Benefit (CR or PR or Stable Disease [SD]) According to RECIST v 1.1

End point title	Percentage of Subjects with Clinical Benefit (CR or PR or Stable Disease [SD]) According to RECIST v 1.1

End point description:

Clinical Benefit was defined as CR plus PR plus SD. CR: disappearance of all target lesions. PR: At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters, in the absence of CR. SD: neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. ITT population 1 included all subjects enrolled in Cohort 1. Only subjects with measurable disease were included in the analysis.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death due to any cause, whichever occurs first (assessed every 12 weeks during treatment period thereafter 28-42 days after the last dose or every 3-6 months up to approximately 47 months)

End point values	Trastuzumab Emtansine (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	1613			
Units: percentage of subjects				
number (not applicable)	47.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) According to RECIST v 1.1

End point title	Duration of Response (DOR) According to RECIST v 1.1

End point description:

DOR is defined as the period from the date of initial confirmed PR or CR (whichever occurs first) until the date of PD or death from any cause. CR: disappearance of all target lesions. PR: At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters, in the absence of CR. PD: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters on study (including baseline). In addition to the relative increase of 20%, the sum of diameters must also demonstrate an absolute increase of >/= 5 millimeters (mm). ITT population 1 included all subjects enrolled in Cohort 1. Only subjects with measurable disease were included in the analysis.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death due to any cause, whichever occurs first (assessed every 12 weeks during treatment period thereafter 28-42 days after the last dose or every 3-6 months up to approximately 47 months)

End point values	Trastuzumab Emtansine (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	1613			
Units: months				
median (confidence interval 95%)	14.1 (12.3 to 15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response According to RECIST v 1.1

End point title	Time to Response According to RECIST v 1.1

End point description:

Time to Response is defined as the time from first dose to first documentation of confirmed PR or CR (whichever occurs first). CR: disappearance of all target lesions. PR: At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters, in the absence of CR. ITT population 1 included all subjects enrolled in Cohort 1. Only responders were included in the

analysis.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death due to any cause, whichever occurs first (assessed every 12 weeks during treatment period thereafter 28-42 days after the last dose or every 3-6 months up to approximately 47 months)

End point values	Trastuzumab Emtansine (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	473			
Units: months				
median (confidence interval 95%)	22.3 (11.8 to 38.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to approximately 47 months	
Adverse event reporting additional description:	
The safety population included all subjects who had received at least 1 dose of study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Trastuzumab Emtansine (All Subjects)

Reporting group description:

This cohort (Cohort 1) enrolled all subjects with HER2-positive, unresectable, LABC or mBC who had received prior anti-HER2 and chemotherapy treatment and had progressed on or after the most recent treatment for LABC or mBC, or within 6 months of completing adjuvant therapy. Subjects received trastuzumab emtansine every 3 weeks until unacceptable toxicity, withdrawal of consent, or disease progression.

Serious adverse events	Trastuzumab Emtansine (All Subjects)		
Total subjects affected by serious adverse events			
subjects affected / exposed	427 / 2002 (21.33%)		
number of deaths (all causes)	1072		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Breast cancer metastatic				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningioma				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to bone				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastatic uterine cancer				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Naevus haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sarcoma				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin neoplasm bleeding				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				

Haematoma				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Circulatory collapse				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hypotension				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vena cava thrombosis				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Breast conserving surgery				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scar excision				

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	13 / 2002 (0.65%)			
occurrences causally related to treatment / all	10 / 14			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	5 / 2002 (0.25%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 5			
General physical health deterioration				
subjects affected / exposed	4 / 2002 (0.20%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	2 / 2			
Chills				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hyperthermia				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Catheter site erythema				

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Implant site dehiscence			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inflammation			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza like illness			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Allergic oedema			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			

Cystocele				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metrorrhagia				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine polyp				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vaginal haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	7 / 2002 (0.35%)			
occurrences causally related to treatment / all	2 / 8			
deaths causally related to treatment / all	0 / 1			
Epistaxis				
subjects affected / exposed	7 / 2002 (0.35%)			
occurrences causally related to treatment / all	3 / 8			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	6 / 2002 (0.30%)			
occurrences causally related to treatment / all	4 / 6			
deaths causally related to treatment / all	1 / 2			

Pneumothorax			
subjects affected / exposed	5 / 2002 (0.25%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	4 / 2002 (0.20%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	1 / 1		
Pleural effusion			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 1		
Pleuritic pain			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Acute pulmonary oedema			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Asthmatic crisis			

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Choking			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Haemoptysis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary fibrosis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pulmonary oedema			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Respiratory tract haemorrhage			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sleep apnoea syndrome			

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	4 / 2002 (0.20%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Agitation			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hallucination			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device breakage			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device extrusion			

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device loosening				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Aspartate aminotransferase increased				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase increased				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Amylase increased				

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ECG signs of myocardial ischaemia				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur fracture				
subjects affected / exposed	8 / 2002 (0.40%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	4 / 2002 (0.20%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				

subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anastomotic ulcer				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Forearm fracture				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hand fracture				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intentional overdose				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic fracture			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation necrosis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Rib fracture			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skeletal injury			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Splenic injury			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac tamponade				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardio-respiratory arrest				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Palpitations				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Epilepsy				
subjects affected / exposed	8 / 2002 (0.40%)			
occurrences causally related to treatment / all	1 / 15			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	7 / 2002 (0.35%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	6 / 2002 (0.30%)			
occurrences causally related to treatment / all	2 / 7			
deaths causally related to treatment / all	2 / 2			
Hemiparesis				

subjects affected / exposed	5 / 2002 (0.25%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	4 / 2002 (0.20%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Cerebral ischaemia				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Leukoencephalopathy				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sciatica				

subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ataxia			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Central nervous system necrosis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
IIIrd nerve paresis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Motor dysfunction			

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorder				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Partial seizures				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vocal cord paralysis				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	13 / 2002 (0.65%)			
occurrences causally related to treatment / all	8 / 14			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	11 / 2002 (0.55%)			
occurrences causally related to treatment / all	11 / 11			
deaths causally related to treatment / all	0 / 0			
Bone marrow failure				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Blindness				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Retinal vein thrombosis				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Vomiting				
subjects affected / exposed	17 / 2002 (0.85%)			
occurrences causally related to treatment / all	10 / 19			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	4 / 2002 (0.20%)			
occurrences causally related to treatment / all	2 / 12			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	5 / 2002 (0.25%)			
occurrences causally related to treatment / all	5 / 6			
deaths causally related to treatment / all	0 / 0			

Gastric haemorrhage			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	4 / 2002 (0.20%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Melaena			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Subileus			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastritis			

subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Abdominal pain upper			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anal haemorrhage			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Abdominal distension			

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal fissure			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric antral vascular ectasia			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis erosive			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroduodenal ulcer			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gingival bleeding			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Glossitis			

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal fistula				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal varices haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Periodontal disease				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Proctalgia				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tooth loss				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatotoxicity				
subjects affected / exposed	7 / 2002 (0.35%)			
occurrences causally related to treatment / all	5 / 7			
deaths causally related to treatment / all	0 / 1			
Hepatic failure				
subjects affected / exposed	5 / 2002 (0.25%)			
occurrences causally related to treatment / all	1 / 5			
deaths causally related to treatment / all	0 / 3			
Cholecystitis				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nodular regenerative hyperplasia				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Cholestasis				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Portal hypertension				

subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Hepatic function abnormal				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hepatic pain				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Non-cirrhotic portal hypertension				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Spider naevus				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal failure				
subjects affected / exposed	4 / 2002 (0.20%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	1 / 3			
Haematuria				

subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Nephrolithiasis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal injury			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperthyroidism			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Musculoskeletal chest pain			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Arthralgia			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Spinal pain			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone lesion			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Kyphosis			

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mobility decreased				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle haemorrhage				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Systemic lupus erythematosus				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	16 / 2002 (0.80%)			
occurrences causally related to treatment / all	1 / 17			
deaths causally related to treatment / all	0 / 2			
Urinary tract infection				

subjects affected / exposed	11 / 2002 (0.55%)			
occurrences causally related to treatment / all	1 / 12			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	8 / 2002 (0.40%)			
occurrences causally related to treatment / all	1 / 10			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	9 / 2002 (0.45%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	9 / 2002 (0.45%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	9 / 2002 (0.45%)			
occurrences causally related to treatment / all	1 / 9			
deaths causally related to treatment / all	1 / 2			
Lung infection				
subjects affected / exposed	6 / 2002 (0.30%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	4 / 2002 (0.20%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Otitis media			
subjects affected / exposed	3 / 2002 (0.15%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Breast cellulitis			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Mastitis			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peritonitis			

subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Pyelonephritis			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis chronic			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal sepsis			
subjects affected / exposed	2 / 2002 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Abscess			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acinetobacter infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis infective			

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacterial infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacterial sepsis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Brain abscess			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Catheter site infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalitis			

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis norovirus			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal viral infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infectious pleural effusion			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infective exacerbation of bronchiectasis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Klebsiella bacteraemia			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Listeriosis			

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver abscess				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumococcal infection				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia streptococcal				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection viral			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal infection			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheobronchitis			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			

subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vulval abscess				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	3 / 2002 (0.15%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Decreased appetite				
subjects affected / exposed	2 / 2002 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Failure to thrive				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hyperuricaemia				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	1 / 2002 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				

subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 2002 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Trastuzumab Emtansine (All Subjects)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1711 / 2002 (85.46%)		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	136 / 2002 (6.79%)		
occurrences (all)	156		
Weight decreased			
subjects affected / exposed	106 / 2002 (5.29%)		
occurrences (all)	109		
Nervous system disorders			
Headache			
subjects affected / exposed	454 / 2002 (22.68%)		
occurrences (all)	650		
Paraesthesia			
subjects affected / exposed	128 / 2002 (6.39%)		
occurrences (all)	139		
Dizziness			
subjects affected / exposed	117 / 2002 (5.84%)		
occurrences (all)	137		
Peripheral sensory neuropathy			
subjects affected / exposed	113 / 2002 (5.64%)		
occurrences (all)	132		
Dysgeusia			

subjects affected / exposed	102 / 2002 (5.09%)		
occurrences (all)	118		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	556 / 2002 (27.77%)		
occurrences (all)	846		
Asthenia			
subjects affected / exposed	492 / 2002 (24.58%)		
occurrences (all)	829		
Pyrexia			
subjects affected / exposed	339 / 2002 (16.93%)		
occurrences (all)	531		
Influenza like illness			
subjects affected / exposed	107 / 2002 (5.34%)		
occurrences (all)	161		
Oedema peripheral			
subjects affected / exposed	102 / 2002 (5.09%)		
occurrences (all)	115		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	165 / 2002 (8.24%)		
occurrences (all)	257		
Anaemia			
subjects affected / exposed	173 / 2002 (8.64%)		
occurrences (all)	231		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	651 / 2002 (32.52%)		
occurrences (all)	1204		
Constipation			
subjects affected / exposed	394 / 2002 (19.68%)		
occurrences (all)	568		
Vomiting			
subjects affected / exposed	294 / 2002 (14.69%)		
occurrences (all)	408		

Diarrhoea subjects affected / exposed occurrences (all)	252 / 2002 (12.59%) 376		
Dry mouth subjects affected / exposed occurrences (all)	283 / 2002 (14.14%) 303		
Stomatitis subjects affected / exposed occurrences (all)	160 / 2002 (7.99%) 213		
Abdominal pain subjects affected / exposed occurrences (all)	139 / 2002 (6.94%) 182		
Abdominal pain upper subjects affected / exposed occurrences (all)	135 / 2002 (6.74%) 163		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	402 / 2002 (20.08%) 669		
Cough subjects affected / exposed occurrences (all)	220 / 2002 (10.99%) 256		
Dyspnoea subjects affected / exposed occurrences (all)	213 / 2002 (10.64%) 237		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	118 / 2002 (5.89%) 134		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	265 / 2002 (13.24%) 349		
Myalgia			

subjects affected / exposed	205 / 2002 (10.24%)		
occurrences (all)	280		
Back pain			
subjects affected / exposed	197 / 2002 (9.84%)		
occurrences (all)	224		
Pain in extremity			
subjects affected / exposed	149 / 2002 (7.44%)		
occurrences (all)	171		
Muscle spasms			
subjects affected / exposed	124 / 2002 (6.19%)		
occurrences (all)	154		
Musculoskeletal pain			
subjects affected / exposed	135 / 2002 (6.74%)		
occurrences (all)	149		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	157 / 2002 (7.84%)		
occurrences (all)	230		
Nasopharyngitis			
subjects affected / exposed	136 / 2002 (6.79%)		
occurrences (all)	195		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	320 / 2002 (15.98%)		
occurrences (all)	398		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported