Clinical trial results:
A randomised, multi-centre, open-label, phase III study of adjuvant lapatinib, trastuzumab, their sequence and their combination in patients with HER2/ErbB2 positive primary breast cancer

Summary

EudraCT number	2006-000562-36
Trial protocol	IE HU FR GB SK EE CZ DK BE DE GR NL IT ES SI BG AT
Global end of trial date	01 July 2021

Results information

Result version number	v2 (current)
This version publication date	06 April 2025
First version publication date	02 July 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CLAP016B2301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00490139
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to compare disease-free survival (DFS) in patients with Human Epidermal Growth Factor Receptor 2 (HER2) overexpressing and/or amplified breast cancer randomized to trastuzumab for one year (Trastuzumab arm) versus lapatinib for one year (Lapatinib arm; this arm was discontinued prior to the primary analysis due to futility) versus weekly trastuzumab (12 or 18 weeks, according to assigned design) followed by a six-week washout period followed by lapatinib (28 or 34 weeks, according to assigned design; Trastuzumab followed by Lapatinib arm) versus trastuzumab in combination with lapatinib for one year (Lapatinib plus Trastuzumab arm).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 May 2007
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	Argentina: 64
Country: Number of subjects enrolled	Australia: 181
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 231
Country: Number of subjects enrolled	Brazil: 98
Country: Number of subjects enrolled	Bulgaria: 26
Country: Number of subjects enrolled	Canada: 42
Country: Number of subjects enrolled	Chile: 108
Country: Number of subjects enrolled	China: 441
Country: Number of subjects enrolled	Czechia: 116
Country: Number of subjects enrolled	Denmark: 187
Country: Number of subjects enrolled	Estonia: 4
Country: Number of subjects enrolled	France: 410
Country: Number of subjects enrolled	Germany: 1375
Country: Number of subjects enrolled	Greece: 56
Country: Number of subjects enrolled	Hong Kong: 56

Country: Number of subjects enrolled	Hungary: 134
Country: Number of subjects enrolled	India: 201
Country: Number of subjects enrolled	Ireland: 52
Country: Number of subjects enrolled	Israel: 47
Country: Number of subjects enrolled	Italy: 371
Country: Number of subjects enrolled	Japan: 142
Country: Number of subjects enrolled	Korea, Republic of: 353
Country: Number of subjects enrolled	Mexico: 31
Country: Number of subjects enrolled	Netherlands: 87
Country: Number of subjects enrolled	New Zealand: 41
Country: Number of subjects enrolled	Norway: 40
Country: Number of subjects enrolled	Pakistan: 204
Country: Number of subjects enrolled	Peru: 143
Country: Number of subjects enrolled	Philippines: 150
Country: Number of subjects enrolled	Poland: 176
Country: Number of subjects enrolled	Romania: 105
Country: Number of subjects enrolled	Russian Federation: 324
Country: Number of subjects enrolled	Singapore: 25
Country: Number of subjects enrolled	Slovakia: 53
Country: Number of subjects enrolled	Slovenia: 20
Country: Number of subjects enrolled	South Africa: 168
Country: Number of subjects enrolled	Spain: 267
Country: Number of subjects enrolled	Switzerland: 56
Country: Number of subjects enrolled	Taiwan: 374
Country: Number of subjects enrolled	Thailand: 172
Country: Number of subjects enrolled	Ukraine: 85
Country: Number of subjects enrolled	United Kingdom: 243
Country: Number of subjects enrolled	United States: 917
Worldwide total number of subjects	8381
EEA total number of subjects	3715

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)	7526
From 65 to 84 years	855
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted in 969 centers in 44 countries worldwide.

Pre-assignment

Screening details:

Based on the IDMC results from 18 August 2011, any patient enrolled onto Lapatinib arm were considered for a new treatment strategy based on discussion with their physician.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Lapatinib plus Trastuzumab

Arm description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: oral lapatinib (OL) 1000 milligrams (mg) daily with trastuzumab (tras) (8 milligrams per kilogram [mg/kg] intravenous [IV] loading dose [LD], followed by 6 mg/kg IV every 3 weeks [E3W]) for 52 weeks (wks). * Design 2: OL 750 mg daily plus wkly tras (4 mg/kg LD, followed by 2 mg/kg IV) concomitantly (conc.) with wkly paclitaxel (pac) 80 mg per squared meter (mg/m^2) IV or docetaxel (doc) 75 mg/m^2 IV E3W for 12 wks. After completion of pac or doc, par. received OL at an increased dose of 1000 mg daily in combination with tras (6 mg/kg without a LD) E3W for 40 wks. * Design 2B: OL 750 mg plus wkly tras (4 mg/kg IV LD, followed by 2 mg/kg IV wkly) conc. with doc 75 mg/m^2 E3W and carboplatin (carb) AUC6 IV for 18 wks. After completion of doc and carb, par. received tras E3W (6 mg/kg without a LD) plus OL 1000 mg daily for 34 wks.

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

Dosage and administration details:

Design 1: Oral lapatinib 1000 mg daily concurrent with trastuzumab 8 mg/kg IV loading dose followed by 6mg/kg IV every 3 weeks (52 weeks total). Design 2: Trastuzumab (4mg/kg loading dose followed by 2mg/kg IV weekly) concurrent with oral lapatinib 750 mg daily and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 every 21 days for 4 cycles (12 weeks). After completion of chemotherapy, the dose of lapatinib will be increased to 1000mg daily concurrently with trastuzumab every 3 weeks (6mg/kg without loading dose) for an additional 40 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concurrently with oral lapatinib 750mg plus weekly trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV. After the completion of chemotherapy, trastuzumab will be administered every 3 weeks (6mg/kg without loading dose) concurrent with lapatinib 1000mg daily for an additional 40 weeks (52 weeks total).

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Trastuzumab (4mg/kg loading dose followed by 2mg/kg IV weekly) concurrent with oral lapatinib 750 mg daily and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2

every 21 days for 4 cycles (12 weeks). After completion of chemotherapy, the dose of lapatinib will be increased to 1000mg daily concurrently with trastuzumab every 3 weeks (6mg/kg without loading dose) for an additional 40 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concurrently with oral lapatinib 750mg plus weekly trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV. After the completion of chemotherapy, trastuzumab will be administered every 3 weeks (6mg/kg without loading dose) concurrent with lapatinib 1000mg daily for an additional 40 weeks (52 weeks total).

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Trastuzumab (4mg/kg loading dose followed by 2mg/kg IV weekly) concurrent with oral lapatinib 750 mg daily and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 every 21 days for 4 cycles (12 weeks). After completion of chemotherapy, the dose of lapatinib will be increased to 1000mg daily concurrently with trastuzumab every 3 weeks (6mg/kg without loading dose) for an additional 40 weeks (52 weeks total).

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 1: Oral lapatinib 1000 mg daily concurrent with trastuzumab 8 mg/kg IV loading dose followed by 6mg/kg IV every 3 weeks (52 weeks total). Design 2: Trastuzumab (4mg/kg loading dose followed by 2mg/kg IV weekly) concurrent with oral lapatinib 750 mg daily and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 every 21 days for 4 cycles (12 weeks). After completion of chemotherapy, the dose of lapatinib will be increased to 1000mg daily concurrently with trastuzumab every 3 weeks (6mg/kg without loading dose) for an additional 40 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concurrently with oral lapatinib 750mg plus weekly trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV. After the completion of chemotherapy, trastuzumab will be administered every 3 weeks (6mg/kg without loading dose) concurrent with lapatinib 1000mg daily for an additional 40 weeks (52 weeks total).

Arm title	Trastuzumab followed by Lapatinib

Arm description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: weekly tras for 12 weeks (4 mg/kg IV loading dose, followed by 2 mg/kg IV weekly), followed by a 6-week washout period, followed by oral lap 1500 mg daily for 34 weeks. * Design 2: weekly tras (4 mg/kg IV loading dose, followed by 2 mg/kg IV) concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks for 12 weeks, followed by a 6-week washout period, followed by oral lap 1500 mg daily for 34 weeks. * Design 2B: weekly tras (4 mg/kg IV loading dose, followed by 2 mg/kg IV weekly) concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV for 18 weeks, followed by a 6-week washout period, followed by oral lap 1500 mg daily for 28 weeks.

Arm type	Experimental
Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 1: Trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) for 12 weeks followed by a 6 week treatment-free interval followed by oral lapatinib 1500mg daily for 34 weeks (52 weeks total). Design 2: Trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) for 12 weeks administered concomitantly and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 every 21 days for 4 cycles; followed by a 6 week treatment-free interval followed by oral lapatinib 1500mg daily for 34 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concomitantly with trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) followed by a 6 week treatment-free interval followed by

oral lapatinib 1500 mg daily for 28 weeks (52 weeks total).

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) for 12 weeks administered concomitantly and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 every 21 days for 4 cycles; followed by a 6 week treatment-free interval followed by oral lapatinib 1500mg daily for 34 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concomitantly with trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) followed by a 6 week treatment-free interval followed by oral lapatinib 1500 mg daily for 28 weeks (52 weeks total).

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) for 12 weeks administered concomitantly and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 every 21 days for 4 cycles; followed by a 6 week treatment-free interval followed by oral lapatinib 1500mg daily for 34 weeks (52 weeks total).

Investigational medicinal product name	Lapatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Design 1: Trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) for 12 weeks followed by a 6 week treatment-free interval followed by oral lapatinib 1500mg daily for 34 weeks (52 weeks total). Design 2: Trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) for 12 weeks administered concomitantly and either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 every 21 days for 4 cycles; followed by a 6 week treatment-free interval followed by oral lapatinib 1500mg daily for 34 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concomitantly with trastuzumab (4mg/kg IV loading dose followed by 2mg/kg IV weekly) followed by a 6 week treatment-free interval followed by oral lapatinib 1500 mg daily for 28 weeks (52 weeks total).

Arm title	Lapatinib

Arm description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: oral lap 1500 mg daily for 52 weeks. * Design 2: oral lap 750 mg daily concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks, for 12 weeks. After completion of paclitaxel or docetaxel, participants received oral lap at an increased dose of 1500 mg daily for 40 weeks. * Design 2B: oral lap 750 mg daily concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV, for 18 weeks. After completion of docetaxel and carboplatin, oral lap was given at an increased dose of 1500 mg for 34 weeks.

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

Dosage and administration details:

Design 1: Lapatinib 1500mg oral daily for a total of 52 weeks. Design 2: Either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 IV every 3 weeks for 4 cycles administered concomitantly with oral lapatinib at 750mg daily. After completion of chemotherapy, oral lapatinib administered at 1500mg daily for an additional 40 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and

carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concomitantly with oral lapatinib at 750mg daily. After completion of chemotherapy, the dose of lapatinib will be increased to 1500mg oral daily for an additional 40 weeks (52 weeks total).

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 IV every 3 weeks for 4 cycles administered concomitantly with oral lapatinib at 750mg daily. After completion of chemotherapy, oral lapatinib administered at 1500mg daily for an additional 40 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concomitantly with oral lapatinib at 750mg daily. After completion of chemotherapy, the dose of lapatinib will be increased to 1500mg oral daily for an additional 40 weeks (52 weeks total).

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 IV every 3 weeks for 4 cycles administered concomitantly with oral lapatinib at 750mg daily. After completion of chemotherapy, oral lapatinib administered at 1500mg daily for an additional 40 weeks (52 weeks total).

Arm title	Trastuzumab

Arm description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: tras 8 mg/kg IV LD, followed by 6 mg/kg IV every 3 weeks for 52 weeks. * Design 2: weekly tras (4 mg/kg IV LD, followed by 2 mg/kg IV weekly) concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks, for 12 weeks. After completion of paclitaxel or docetaxel, participants received tras (6 mg/kg without a LD every 3 weeks for 40 weeks. * Design 2B: weekly tras (4 mg/kg IV LD, followed by 2 mg/kg IV weekly) concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV, for 18 weeks. After completion of docetaxel and carboplatin, participants received tras every 3 weeks (6 mg/kg without a LD) for 34 weeks. "

Arm type	Active comparator
Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 1: Trastuzumab 8mg/kg IV loading dose followed by 6mg/kg IV every 3 weeks for a total of 52 weeks. Design 2: Either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 IV every 3 weeks for 4 cycles administered concomitantly with trastuzumab 4mg/kg IV loading dose followed by 2mg/kg IV weekly. After completion of chemotherapy, trastuzumab administered every 3 weeks (6mg/kg IV without loading dose) for an additional 40 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concomitantly with trastuzumab 4mg/kg IV loading dose followed by 2mg/kg IV weekly. After completion of chemotherapy, trastuzumab (6mg/kg without loading dose) every 3 weeks for an additional 40 weeks (52 weeks total).

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 IV every 3 weeks for 4 cycles administered concomitantly with trastuzumab 4mg/kg IV loading dose followed by 2mg/kg IV weekly. After completion of chemotherapy, trastuzumab administered every 3 weeks (6mg/kg IV

without loading dose) for an additional 40 weeks (52 weeks total). Design 2B: Docetaxel 75mg/m2 and carboplatin AUC 6 every 3 weeks for 6 cycles (18 weeks) administered concomitantly with trastuzumab 4mg/kg IV loading dose followed by 2mg/kg IV weekly. After completion of chemotherapy, trastuzumab (6mg/kg without loading dose) every 3 weeks for an additional 40 weeks (52 weeks total).

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Design 2: Either paclitaxel 80mg/m2 IV weekly for 12 weeks OR docetaxel 75mg/m2 IV every 3 weeks for 4 cycles administered concomitantly with trastuzumab 4mg/kg IV loading dose followed by 2mg/kg IV weekly. After completion of chemotherapy, trastuzumab administered every 3 weeks (6mg/kg IV without loading dose) for an additional 40 weeks (52 weeks total).

Number of subjects in period 1	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib
Started	2093	2091	2100
Safety population	2061	2076	2056
Completed	1132	1184	1179
Not completed	961	907	921
Consent withdrawn by subject	333	322	396
Data unavailable due to regulatory issues	98	96	85
Data unavailable due to lapsed ethical consent	14	13	14
Patient did not sign ICF 12	169	176	139
Lost to follow-up	249	216	205
Other reasons as defined per protocol	98	84	82

Number of subjects in period 1	Trastuzumab
Started	2097
Safety population	2076
Completed	1192
Not completed	905
Consent withdrawn by subject	295
Data unavailable due to regulatory issues	95
Data unavailable due to lapsed ethical consent	14
Patient did not sign ICF 12	167
Lost to follow-up	229
Other reasons as defined per protocol	105

Baseline characteristics

Reporting groups

Reporting group title	Lapatinib plus Trastuzumab

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: oral lapatinib (OL) 1000 milligrams (mg) daily with trastuzumab (tras) (8 milligrams per kilogram [mg/kg] intravenous [IV] loading dose [LD], followed by 6 mg/kg IV every 3 weeks [E3W]) for 52 weeks (wks). * Design 2: OL 750 mg daily plus wkly tras (4 mg/kg LD, followed by 2 mg/kg IV) concomitantly (conc.) with wkly paclitaxel (pac) 80 mg per squared meter (mg/m^2) IV or docetaxel (doc) 75 mg/m^2 IV E3W for 12 wks. After completion of pac or doc, par. received OL at an increased dose of 1000 mg daily in combination with tras (6 mg/kg without a LD) E3W for 40 wks. * Design 2B: OL 750 mg plus wkly tras (4 mg/kg IV LD, followed by 2 mg/kg IV wkly) conc. with doc 75 mg/m^2 E3W and carboplatin (carb) AUC6 IV for 18 wks. After completion of doc and carb, par. received tras E3W (6 mg/kg without a LD) plus OL 1000 mg daily for 34 wks.

Reporting group title	Trastuzumab followed by Lapatinib

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: weekly tras for 12 weeks (4 mg/kg IV loading dose, followed by 2 mg/kg IV weekly), followed by a 6-week washout period, followed by oral lap 1500 mg daily for 34 weeks. * Design 2: weekly tras (4 mg/kg IV loading dose, followed by 2 mg/kg IV) concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks for 12 weeks, followed by a 6-week washout period, followed by oral lap 1500 mg daily for 34 weeks. * Design 2B: weekly tras (4 mg/kg IV loading dose, followed by 2 mg/kg IV weekly) concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV for 18 weeks, followed by a 6-week washout period, followed by oral lap 1500 mg daily for 28 weeks.

Reporting group title	Lapatinib

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: oral lap 1500 mg daily for 52 weeks. * Design 2: oral lap 750 mg daily concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks, for 12 weeks. After completion of paclitaxel or docetaxel, participants received oral lap at an increased dose of 1500 mg daily for 40 weeks. * Design 2B: oral lap 750 mg daily concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV, for 18 weeks. After completion of docetaxel and carboplatin, oral lap was given at an increased dose of 1500 mg for 34 weeks.

Reporting group title	Trastuzumab

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: tras 8 mg/kg IV LD, followed by 6 mg/kg IV every 3 weeks for 52 weeks. * Design 2: weekly tras (4 mg/kg IV LD, followed by 2 mg/kg IV weekly) concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks, for 12 weeks. After completion of paclitaxel or docetaxel, participants received tras (6 mg/kg without a LD every 3 weeks for 40 weeks. * Design 2B: weekly tras (4 mg/kg IV LD, followed by 2 mg/kg IV weekly) concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV, for 18 weeks. After completion of docetaxel and carboplatin, participants received tras every 3 weeks (6 mg/kg without a LD) for 34 weeks. "

Reporting group values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib
Number of subjects	2093	2091	2100
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0

Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1879	1877	1889
From 65-84 years	214	214	211
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	2091	2086	2098
Male	2	5	2
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	48	45	47
Asian: Central/South	107	103	110
Asian: East	311	312	299
Asian: Japanese	33	36	33
Asian: South East	95	92	107
Black or African American	38	30	43
Native Hawaiian or Other Pacific	2	4	4
White: Arabic	53	52	62
White: Caucasian	1392	1402	1372
Other Race	14	14	23
Unknown/Missing	0	1	0
Axillary Lymph Node Status			
Axillary Lymph Node Status was categorized as: a) Not applicable (neoadjuvant chemotherapy); b) Node negative (no neoadjuvant chemotherapy); c) 1-3 positive nodes (no neoadjuvant chemotherapy); d) >= 4 positive nodes (no neoadjuvant chemotherapy)			
Units: Subjects			
Not applicable (neoadjuvant chemotherapy)	168	170	167
Node negative (no neoadjuvant chemotherapy)	845	842	841
1-3 positive nodes (no neoadjuvant chemotherapy)	617	617	620
>= 4 positive nodes (no neoadjuvant chemotherapy)	463	462	472
Timing of Chemotherapy			
Timing of (neo)adjuvant chemotherapy was defined as follows: Design 1 – sequentially (all chemotherapy completed prior to randomization) versus Design 2 – concurrently with targeted therapy (taxane medication administered with targeted treatment after randomization). Subjects treated concurrently but without anthracycline (Design 2B) were regarded as part of Design 2 for all stratified analyses.			
Units: Subjects			
Sequential	1155	1143	1168
Concurrent	938	948	932
Hormone Receptor (HR) Status			
HR status was determined from the percentage of Estrogen Receptor (ER) and Progesterone Receptor (PgR) cells stained positive: a) Positive: if the percentage of cells stained positive is >= 1% for either ER or PgR; b) Negative: if the percentage of cells stained positive is < 1% for both ER and PgR			
Units: Subjects			
Negative	890	886	903
Positive	1203	1205	1197
GenderNIH Units: Subjects			
Female	2091	2086	2098
Male	2	5	2

AgeContinuous			
Units: years			
arithmetic mean	50.9	50.8	51.2
standard deviation	± 10.23	± 10.32	± 10.18

Reporting group values	Trastuzumab	Total	
Number of subjects	2097	8381	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1881	7526	
From 65-84 years	216	855	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	2097	8372	
Male	0	9	
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	47	187	
Asian: Central/South	109	429	
Asian: East	314	1236	
Asian: Japanese	43	145	
Asian: South East	89	383	
Black or African American	25	136	
Native Hawaiian or Other Pacific	5	15	
White: Arabic	69	236	
White: Caucasian	1382	5548	
Other Race	14	65	
Unknown/Missing	0	1	
Axillary Lymph Node Status			
Axillary Lymph Node Status was categorized as: a) Not applicable (neoadjuvant chemotherapy); b) Node negative (no neoadjuvant chemotherapy); c) 1-3 positive nodes (no neoadjuvant chemotherapy); d) >= 4 positive nodes (no neoadjuvant chemotherapy)			
Units: Subjects			
Not applicable (neoadjuvant chemotherapy)	181	686	
Node negative (no neoadjuvant chemotherapy)	844	3372	
1-3 positive nodes (no neoadjuvant chemotherapy)	603	2457	
>= 4 positive nodes (no neoadjuvant chemotherapy)	469	1866	
Timing of Chemotherapy			
Timing of (neo)adjuvant chemotherapy was defined as follows: Design 1 – sequentially (all chemotherapy completed prior to randomization) versus Design 2 – concurrently with targeted therapy (taxane medication administered with targeted treatment after randomization). Subjects treated concurrently but without anthracycline (Design 2B) were regarded as part of Design 2 for all stratified			

analyses.			
Units: Subjects			
Sequential	1147	4613	
Concurrent	950	3768	
Hormone Receptor (HR) Status			
HR status was determined from the percentage of Estrogen Receptor (ER) and Progesterone Receptor (PgR) cells stained positive: a) Positive: if the percentage of cells stained positive is >= 1% for either ER or PgR; b) Negative: if the percentage of cells stained positive is < 1% for both ER and PgR			
Units: Subjects			
Negative	897	3576	
Positive	1200	4805	
GenderNIH			
Units: Subjects			
Female	2097	8372	
Male	0	9	
AgeContinuous			
Units: years			
arithmetic mean	51.0		
standard deviation	± 10.25	-	

End points

End points reporting groups

Reporting group title	Lapatinib plus Trastuzumab

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: oral lapatinib (OL) 1000 milligrams (mg) daily with trastuzumab (tras) (8 milligrams per kilogram [mg/kg] intravenous [IV] loading dose [LD], followed by 6 mg/kg IV every 3 weeks [E3W]) for 52 weeks (wks). * Design 2: OL 750 mg daily plus wkly tras (4 mg/kg LD, followed by 2 mg/kg IV) concomitantly (conc.) with wkly paclitaxel (pac) 80 mg per squared meter (mg/m^2) IV or docetaxel (doc) 75 mg/m^2 IV E3W for 12 wks. After completion of pac or doc, par. received OL at an increased dose of 1000 mg daily in combination with tras (6 mg/kg without a LD) E3W for 40 wks. * Design 2B: OL 750 mg plus wkly tras (4 mg/kg IV LD, followed by 2 mg/kg IV wkly) conc. with doc 75 mg/m^2 E3W and carboplatin (carb) AUC6 IV for 18 wks. After completion of doc and carb, par. received tras E3W (6 mg/kg without a LD) plus OL 1000 mg daily for 34 wks.

Reporting group title	Trastuzumab followed by Lapatinib

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: weekly tras for 12 weeks (4 mg/kg IV loading dose, followed by 2 mg/kg IV weekly), followed by a 6-week washout period, followed by oral lap 1500 mg daily for 34 weeks. * Design 2: weekly tras (4 mg/kg IV loading dose, followed by 2 mg/kg IV) concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks for 12 weeks, followed by a 6-week washout period, followed by oral lap 1500 mg daily for 34 weeks. * Design 2B: weekly tras (4 mg/kg IV loading dose, followed by 2 mg/kg IV weekly) concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV for 18 weeks, followed by a 6-week washout period, followed by oral lap 1500 mg daily for 28 weeks.

Reporting group title	Lapatinib

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: oral lap 1500 mg daily for 52 weeks. * Design 2: oral lap 750 mg daily concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks, for 12 weeks. After completion of paclitaxel or docetaxel, participants received oral lap at an increased dose of 1500 mg daily for 40 weeks. * Design 2B: oral lap 750 mg daily concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV, for 18 weeks. After completion of docetaxel and carboplatin, oral lap was given at an increased dose of 1500 mg for 34 weeks.

Reporting group title	Trastuzumab

Reporting group description:

Participants received treatment per one of three designs and adjuvant radiotherapy / adjuvant anti-estrogen therapy when clinically indicated. * Design 1: tras 8 mg/kg IV LD, followed by 6 mg/kg IV every 3 weeks for 52 weeks. * Design 2: weekly tras (4 mg/kg IV LD, followed by 2 mg/kg IV weekly) concomitantly with weekly paclitaxel 80 mg/m^2 IV or docetaxel 75 mg/m^2 IV every 3 weeks, for 12 weeks. After completion of paclitaxel or docetaxel, participants received tras (6 mg/kg without a LD every 3 weeks for 40 weeks. * Design 2B: weekly tras (4 mg/kg IV LD, followed by 2 mg/kg IV weekly) concomitantly with docetaxel 75 mg/m^2 every 3 weeks and carboplatin AUC6 IV, for 18 weeks. After completion of docetaxel and carboplatin, participants received tras every 3 weeks (6 mg/kg without a LD) for 34 weeks. "

Primary: Disease-Free Survival (DFS) at the Primary Analysis

End point title	Disease-Free Survival (DFS) at the Primary Analysis

End point description:

Disease-Free Survival (DFS) was defined as the interval between randomization and the date of first occurrence of disease recurrence (local, regional or distant), a contralateral invasive breast cancer, a second primary cancer or death without recurrence. Only deaths occurring in participants whose clinical follow-up was ongoing at the time of death and who had no recurrence, contralateral breast cancer (CBC) or second primary malignancy (SPM) reported prior to death were considered as death without recurrence. DFS was estimated using the Kaplan Meier method. The percentile data values presented here indicate the percentage (95, 90, 85, 80 and 75 percent) of participants who had disease free survival for the indicated years.

End point type	Primary

End point timeframe:

From randomization until the date of the first occurrence of disease recurrence, a contralateral invasive breast cancer, a second primary cancer, or death from any cause (median follow-up of 4.5 years)

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	2100	2097
Units: Years				
number (not applicable)				
95th Percentile	1.9	1.3	1.0	1.5
90th Percentile	3.2	2.8	1.8	2.6
85th Percentile	5.1	4.8	2.8	4.2
80th Percentile	6.1	999	999	5.6
75th Percentile	6.1	999	999	999

Statistical analyses

Statistical analysis title	DFS at the Primary Analysis
Comparison groups	Trastuzumab followed by Lapatinib v Trastuzumab
Number of subjects included in analysis	4188
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.61
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.13

Statistical analysis title	DFS at the Primary Analysis
Comparison groups	Lapatinib plus Trastuzumab v Trastuzumab
Number of subjects included in analysis	4190
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.048
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1

Secondary: Disease-Free Survival (DFS) at the 10-Year Follow-Up

End point title	Disease-Free Survival (DFS) at the 10-Year Follow-Up

End point description:

Disease-Free Survival (DFS) was defined as the interval between randomization and the date of first occurrence of disease recurrence (local, regional or distant), a contralateral invasive breast cancer, a second primary cancer or death without recurrence. Only deaths occurring in participants whose clinical follow-up was ongoing at the time of death and who had no recurrence, contralateral breast cancer (CBC) or second primary malignancy (SPM) reported prior to death were considered as death without recurrence. DFS was estimated using the Kaplan
Meier method. The percentile data values presented here indicate the percentage (95, 90, 85 and 80 percent) of participants who had disease free survival for the indicated years.

End point type	Secondary

End point timeframe:

From randomization until the date of the first occurrence of disease recurrence, a contralateral invasive breast cancer, a second primary cancer, or death from any cause, assessed up to approximately 10 years

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	0[1]	2097
Units: Years				
number (not applicable)				
95th Percentile	1.89	1.27		1.49
90th Percentile	3.21	2.80		2.63
85th Percentile	5.92	4.85		4.43
80th Percentile	8.99	9.18		7.42

Notes:

[1] - The Lapatinib alone arm was discontinued prior to primary analysis due to futility.

Statistical analyses

Statistical analysis title	DFS at the 10-Year Follow-Up
Comparison groups	Trastuzumab followed by Lapatinib v Trastuzumab
Number of subjects included in analysis	4188
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.914

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.05

Statistical analysis title	DFS at the 10-Year Follow-Up
Comparison groups	Lapatinib plus Trastuzumab v Trastuzumab
Number of subjects included in analysis	4190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.887
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.02

Secondary: Overall Survival (OS) at the Primary Analysis

End point title	Overall Survival (OS) at the Primary Analysis

End point description:

Overall Survival (OS) was defined as the time from randomization until death due to any cause. Participants who had not died were censored at the last date they were known to be alive, or date of withdrawal of consent. OS was calculated in years as (date of death minus the date of randomization +1) divided by 365.25. The percentile data values presented here indicate the percentage (99, 98, 97, 96, 95 and 90 percent) of participants who survived for the indicated years.

End point type	Secondary

End point timeframe:

From randomization until death due to any cause (median follow-up of 4.5 years)

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	0[2]	2097
Units: Years				
number (not applicable)				
99th Percentile	1.7	1.2		1.7
98th Percentile	2.2	1.6		2.1
97th Percentile	2.8	2.2		2.6
96th Percentile	3.4	2.9		3.0
95th Percentile	3.9	3.7		3.6
90th Percentile	999	999		5.9

Notes:
[2] - The Lapatinib alone arm was discontinued prior to primary analysis due to futility.

Statistical analyses

Statistical analysis title	OS at the Primary Analysis
Comparison groups	Trastuzumab followed by Lapatinib v Trastuzumab
Number of subjects included in analysis	4188
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.433
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.16

Statistical analysis title	OS at the Primary Analysis
Comparison groups	Lapatinib plus Trastuzumab v Trastuzumab
Number of subjects included in analysis	4190
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.078
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.03

Secondary: Overall Survival (OS) at the 10-Year Follow-Up

End point title	Overall Survival (OS) at the 10-Year Follow-Up

End point description:

Overall Survival (OS) was defined as the time from randomization until death due to any cause. Participants who had not died were censored at the last date they were known to be alive, or date of withdrawal of consent. OS was calculated in years as (date of death minus the date of randomization +1) divided by 365.25. The percentile data values presented here indicate the percentage (99, 98, 95 and 90 percent) of participants who survived for the indicated years.

End point type	Secondary

End point timeframe:

From randomization until death due to any cause, assessed up to approximately 10 years

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	0[3]	2097
Units: Years				
number (not applicable)				
99th Percentile	1.68	1.17		1.75
98th Percentile	2.19	1.60		2.07
95th Percentile	3.92	3.52		3.65
90th Percentile	8.31	8.49		6.72

Notes:

[3] - The Lapatinib alone arm was discontinued prior to primary analysis due to futility.

Statistical analyses

Statistical analysis title	OS at the 10-Year Follow-Up
Comparison groups	Trastuzumab followed by Lapatinib v Trastuzumab
Number of subjects included in analysis	4188
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.863
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.04

Statistical analysis title	OS at the 10-Year Follow-Up
Comparison groups	Lapatinib plus Trastuzumab v Trastuzumab
Number of subjects included in analysis	4190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.853
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.03

Secondary: Analysis of Time to Recurrence (TTR)

End point title	Analysis of Time to Recurrence (TTR)

End point description:

Time to Recurrence (TTR) was defined as the the time from randomization to breast cancer recurrence, ignoring second primary cancers (including contralateral breast cancers and non-breast second malignancies) and counting deaths without recurrence as a competing risk.

End point type	Secondary

End point timeframe:

From randomization until the date of the first occurrence of a disease recurrence, assessed up to approximately 10 years

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	0[4]	2097
Units: Participants				
Local, regional, or distant recurrence	243	275		298
Death as a competing risk	43	38		46
Censored	1807	1778		1753

Notes:

[4] - The Lapatinib alone arm was discontinued prior to primary analysis due to futility.

Statistical analyses

Statistical analysis title	Time to Recurrence (TTR)
Comparison groups	Trastuzumab followed by Lapatinib v Trastuzumab
Number of subjects included in analysis	4188
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.1

Statistical analysis title	Time to Recurrence (TTR)
Comparison groups	Lapatinib plus Trastuzumab v Trastuzumab

Number of subjects included in analysis	4190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.811
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.96

Secondary: Analysis of Time to Distant Recurrence (TTDR)

End point title	Analysis of Time to Distant Recurrence (TTDR)

End point description:

Time to Distant Recurrence (TTDR) was defined as the the time from randomization to first distant breast cancer recurrence, ignoring locoregional recurrences and second primary cancers, (including contralateral breast cancers and non-breast second malignancies) and counting deaths without recurrence as a competing risk.

End point type	Secondary

End point timeframe:

From randomization until the date of the first occurrence of distant recurrence, assessed up to approximately 10 years

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	0[5]	2097
Units: Participants				
Distant recurrence	213	238		250
Death as a competing risk	45	41		54
Censored	1835	1812		1793

Notes:

[5] - The Lapatinib alone arm was discontinued prior to primary analysis due to futility.

Statistical analyses

Statistical analysis title	Time to Distant Recurrence (TTDR)
Comparison groups	Trastuzumab followed by Lapatinib v Trastuzumab
Number of subjects included in analysis	4188
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.968

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.16

Statistical analysis title	Time to Distant Recurrence (TTDR)
Comparison groups	Lapatinib plus Trastuzumab v Trastuzumab
Number of subjects included in analysis	4190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.852
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.02

Secondary: Analysis of Time to Central Nervous System (CNS) Recurrence

End point title	Analysis of Time to Central Nervous System (CNS) Recurrence

End point description:

Time to Central Nervous System (CNS) recurrence was defined as the time from randomization to first CNS recurrence. Both brain metastasis and meningitis carcinomatosa were considered.

End point type	Secondary

End point timeframe:

From randomization until the first central nervous system recurrence, assessed up to approximately 10 years

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	0[6]	2097
Units: Participants				
CNS recurrence	91	91		95
Death as a competing risk	114	117		142
Censored	1888	1883		1860

Notes:

[6] - The Lapatinib alone arm was discontinued prior to primary analysis due to futility.

Statistical analyses

Statistical analysis title	Time to CNS Recurrence
Comparison groups	Trastuzumab followed by Lapatinib v Trastuzumab
Number of subjects included in analysis	4188
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.31

Statistical analysis title	Time to CNS Recurrence
Comparison groups	Lapatinib plus Trastuzumab v Trastuzumab
Number of subjects included in analysis	4190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.986
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.31

Secondary: Cumulative incidence of brain metastases

End point title	Cumulative incidence of brain metastases

End point description:

The cumulative incidence of brain metastases as the first site of breast cancer recurrence among treatment arms was assessed using a hierarchy of primary type and location of first DFS event in cases where more than one event was identified simultaneously. Because diagnostic procedures for different types of recurrence could not be performed on exactly the same day, any diagnoses noted within a two month (60 day) period of the first reported event was considered as identified simultaneously for purposes of defining the type of the first event and the date of event was be regarded as the earliest of the relevant events.

End point type	Secondary

End point timeframe:

From randomization until the date of the first occurrence of a disease recurrence, assessed up to approximately 10 years

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	0[7]	2097
Units: Participants	50	52		48

Notes:

[7] - The Lapatinib alone arm was discontinued prior to primary analysis due to futility.

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

Pre-treatment deaths were collected from day of participant's informed consent to the day before first dose of study medication.
On-treatment deaths were collected from first dose of study medication to 30 days after last dose of study medication (on-treatment), up to approximately 56 weeks.
Deaths were collected in the post treatment survival follow up from 31 days after last dose of study medication until the end of the study, up to approximately 10 years.

End point type	Post-hoc

End point timeframe:

Pre-treatment deaths: Up to 14 days prior to treatment. On-treatment deaths: Up to 56 weeks. Post-treatment deaths: up to 10 years.

End point values	Lapatinib plus Trastuzumab	Trastuzumab followed by Lapatinib	Lapatinib	Trastuzumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2093	2091	2100	2097
Units: Participants				
Pre-treatment deaths	1	2	1	2
On-treatment deaths	6	5	12	3
Post-treatment deaths	189	190	250	228
All deaths	196	197	263	233

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events (AEs) were collected from first dose of study medication until the last dose plus 30 days post-treat follow-up, assessed up to approximately 56 weeks.	
Adverse event reporting additional description:	
Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Lapatinib plus Trastuzumab
Reporting group description:	
Lapatinib plus Trastuzumab: Events up to 30 days post-treatment	
Reporting group title	Lapatinib
Reporting group description:	
Lapatinib: Events up to 30 days post-treatment	
Reporting group title	Trastuzumab
Reporting group description:	
Trastuzumab: Events up to 30 days post-treatment	
Reporting group title	Trastuzumab followed by Lapatinib
Reporting group description:	
Trastuzumab followed by Lapatinib: Events up to 30 days post-treatment	

Serious adverse events	Lapatinib plus Trastuzumab	Lapatinib	Trastuzumab
Total subjects affected by serious adverse events			
subjects affected / exposed	379 / 2061 (18.39%)	394 / 2056 (19.16%)	251 / 2076 (12.09%)
number of deaths (all causes)	6	12	3
number of deaths resulting from adverse events	2	3	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE LYMPHOCYTIC LEUKAEMIA			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
ACUTE PROMYELOCYTIC LEUKAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL CARCINOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL STROMAL TUMOUR			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMANGIOMA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN BREAST NEOPLASM			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BENIGN OVARIAN TUMOUR			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC CANCER			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BORDERLINE OVARIAN TUMOUR			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER			
subjects affected / exposed	3 / 2061 (0.15%)	3 / 2056 (0.15%)	4 / 2076 (0.19%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CANCER IN SITU			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER NEOPLASM			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRADUCTAL PAPILLOMA OF BREAST			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEIOMYOMA			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEIOMYOSARCOMA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGIOMA BENIGN			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOMA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGIOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LENTIGO MALIGNA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTASES TO CENTRAL NERVOUS SYSTEM			

subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
NEUROENDOCRINE TUMOUR			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN ADENOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN CANCER			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN GERM CELL TERATOMA BENIGN			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL CANCER			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATIC CARCINOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PAPILLARY THYROID CANCER			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARATHYROID TUMOUR BENIGN			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLASMA CELL MYELOMA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN NEOPLASM			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL CELL LUNG CANCER			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF THE VULVA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERFICIAL SPREADING MELANOMA STAGE UNSPECIFIED			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THYROID CANCER			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE CANCER			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOTENSION			
subjects affected / exposed	2 / 2061 (0.10%)	2 / 2056 (0.10%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JUGULAR VEIN THROMBOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSIVE CRISIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CIRCULATORY COLLAPSE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			
subjects affected / exposed	2 / 2061 (0.10%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM VENOUS			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLUSHING			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENOUS THROMBOSIS LIMB			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR INSUFFICIENCY			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOSIS			
subjects affected / exposed	2 / 2061 (0.10%)	1 / 2056 (0.05%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	1 / 2	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERFICIAL VEIN THROMBOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCLAVIAN VEIN THROMBOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHEUMATOID VASCULITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORTHOSTATIC HYPOTENSION			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ADVERSE DRUG REACTION			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASTHENIA			
subjects affected / exposed	2 / 2061 (0.10%)	4 / 2056 (0.19%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	2 / 2	4 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	1 / 2061 (0.05%)	2 / 2056 (0.10%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHILLS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC FATIGUE SYNDROME			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
GRANULOMA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FAT NECROSIS			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	5 / 2061 (0.24%)	7 / 2056 (0.34%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	5 / 5	6 / 7	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEELING COLD			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED THROMBOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPAIRED HEALING			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPLANT SITE THROMBOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLAMMATION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPOGRANULOMA			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALAISE			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NECROSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OEDEMA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUCOSAL INFLAMMATION			
subjects affected / exposed	2 / 2061 (0.10%)	3 / 2056 (0.15%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			

subjects affected / exposed	11 / 2061 (0.53%)	13 / 2056 (0.63%)	5 / 2076 (0.24%)
occurrences causally related to treatment / all	6 / 13	4 / 13	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUDDEN DEATH			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
SARCOIDOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAPHYLACTIC REACTION			
subjects affected / exposed	3 / 2061 (0.15%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAPHYLACTOID REACTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 2061 (0.05%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSENSITIVITY			
subjects affected / exposed	4 / 2061 (0.19%)	1 / 2056 (0.05%)	4 / 2076 (0.19%)
occurrences causally related to treatment / all	4 / 4	0 / 1	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
BREAST HAEMATOMA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ADENOMYOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CALCIFICATIONS			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST DISORDER			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST FIBROSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST INFLAMMATION			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST NECROSIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST SWELLING			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL HYPERPLASIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTERINE POLYP			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN CYST			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN CYST RUPTURED			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC PAIN			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTMENOPAUSAL HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERMENSTRUAL BLEEDING			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATELECTASIS			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHIECTASIS			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOPTYSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHONIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	4 / 2061 (0.19%)	2 / 2056 (0.10%)	6 / 2076 (0.29%)
occurrences causally related to treatment / all	2 / 4	2 / 2	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COUGH			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	2 / 2061 (0.10%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARYNGEAL OEDEMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG CONSOLIDATION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG DISORDER			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURISY			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURITIC PAIN			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONITIS			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	5 / 2076 (0.24%)
occurrences causally related to treatment / all	0 / 0	2 / 2	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFILTRATION			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 2061 (0.10%)	6 / 2056 (0.29%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	2 / 2	3 / 6	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PULMONARY GRANULOMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY MASS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY OEDEMA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY THROMBOSIS			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Psychiatric disorders			
RESTLESSNESS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDE ATTEMPT			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABNORMAL BEHAVIOUR			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL DISORDER			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMPLETED SUICIDE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSION			

subjects affected / exposed	3 / 2061 (0.15%)	1 / 2056 (0.05%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
INSOMNIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MAJOR DEPRESSION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL WITHDRAWAL SYNDROME			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
THROMBOSIS IN DEVICE			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE DISLOCATION			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE EXPULSION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALANINE AMINOTRANSFERASE			

INCREASED			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMYLASE INCREASED			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD MAGNESIUM DECREASED			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD POTASSIUM DECREASED			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD UREA INCREASED			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COAGULATION TEST ABNORMAL			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EASTERN COOPERATIVE ONCOLOGY GROUP PERFORMANCE STATUS WORSENED			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ELECTROCARDIOGRAM ABNORMAL			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BODY TEMPERATURE INCREASED			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ELECTROCARDIOGRAM T WAVE INVERSION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	2 / 2061 (0.10%)	3 / 2056 (0.15%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	2 / 2	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPASE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLATELET COUNT DECREASED			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WEIGHT DECREASED			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIPASE INCREASED			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
CONTUSION			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ALCOHOL POISONING			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ANKLE FRACTURE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARBON MONOXIDE POISONING			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONCUSSION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FIBULA FRACTURE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOT FRACTURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOREIGN BODY			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURE			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURED COCCYX			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER LIMB FRACTURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUMERUS FRACTURE			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIGAMENT INJURY			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTIPLE INJURIES			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC FRACTURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIATION FIBROSIS - LUNG			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIATION PNEUMONITIS			
subjects affected / exposed	1 / 2061 (0.05%)	2 / 2056 (0.10%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIATION SKIN INJURY			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RADIUS FRACTURE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SEROMA			

subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL FRACTURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STERNAL FRACTURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THERMAL BURN			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TIBIA FRACTURE			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER LIMB FRACTURE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			

subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND COMPLICATION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
GILBERT'S SYNDROME			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL THROMBOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL TACHYCARDIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ATRIAL FIBRILLATION			
subjects affected / exposed	5 / 2061 (0.24%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	3 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ARRHYTHMIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	24 / 2061 (1.16%)	7 / 2056 (0.34%)	19 / 2076 (0.92%)
occurrences causally related to treatment / all	24 / 24	4 / 7	19 / 19
deaths causally related to treatment / all	1 / 1	1 / 1	1 / 1
ACUTE CORONARY SYNDROME			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	2 / 2061 (0.10%)	1 / 2056 (0.05%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	1 / 2	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	3 / 2061 (0.15%)	4 / 2056 (0.19%)	4 / 2076 (0.19%)
occurrences causally related to treatment / all	3 / 3	3 / 4	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRACARDIAC THROMBUS			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOMYOPATHY			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC VENTRICULAR THROMBOSIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALPITATIONS			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
AMYOTROPHIC LATERAL SCLEROSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRAIN HYPOXIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBELLAR ATAXIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPILEPSY			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACIAL PARALYSIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	2 / 2061 (0.10%)	3 / 2056 (0.15%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 2	2 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOTONIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOTOR NEURONE DISEASE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROPATHY PERIPHERAL			

subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRACRANIAL ANEURYSM			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POLYNEUROPATHY			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
QUADRIPARESIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	2 / 2061 (0.10%)	3 / 2056 (0.15%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEROTONIN SYNDROME			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOMNOLENCE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			

subjects affected / exposed	2 / 2061 (0.10%)	3 / 2056 (0.15%)	5 / 2076 (0.24%)
occurrences causally related to treatment / all	1 / 2	1 / 3	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT GLOBAL AMNESIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	20 / 2061 (0.97%)	13 / 2056 (0.63%)	7 / 2076 (0.34%)
occurrences causally related to treatment / all	23 / 23	13 / 13	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	2 / 2061 (0.10%)	2 / 2056 (0.10%)	7 / 2076 (0.34%)
occurrences causally related to treatment / all	2 / 2	2 / 2	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCYTOPENIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	37 / 2061 (1.80%)	36 / 2056 (1.75%)	20 / 2076 (0.96%)
occurrences causally related to treatment / all	49 / 49	37 / 37	24 / 24
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAEMIA			

subjects affected / exposed	7 / 2061 (0.34%)	13 / 2056 (0.63%)	7 / 2076 (0.34%)
occurrences causally related to treatment / all	7 / 8	11 / 13	5 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EOSINOPHILIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	10 / 2061 (0.49%)	12 / 2056 (0.58%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	9 / 10	12 / 13	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AGRANULOCYTOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTIGO			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TINNITUS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
DIPLOPIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RETINAL DETACHMENT			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIORBITAL OEDEMA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL FISSURE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	4 / 2061 (0.19%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	3 / 4	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL MASS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL DISTENSION			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN			
subjects affected / exposed	6 / 2061 (0.29%)	4 / 2056 (0.19%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	5 / 7	3 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS EROSIVE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	53 / 2061 (2.57%)	44 / 2056 (2.14%)	9 / 2076 (0.43%)
occurrences causally related to treatment / all	56 / 58	46 / 48	6 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENAL ULCER			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPEPSIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPIPLOIC APPENDAGITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS			
subjects affected / exposed	2 / 2061 (0.10%)	1 / 2056 (0.05%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	1 / 2	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL PERFORATION			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL TOXICITY			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL ULCER			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHOIDS			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	4 / 2076 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	5 / 2061 (0.24%)	7 / 2056 (0.34%)	6 / 2076 (0.29%)
occurrences causally related to treatment / all	4 / 5	6 / 7	6 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
REFLUX GASTRITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STOMATITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOLVULUS			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	9 / 2061 (0.44%)	9 / 2056 (0.44%)	8 / 2076 (0.39%)
occurrences causally related to treatment / all	8 / 10	8 / 9	4 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
BILE DUCT STENOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILIARY COLIC			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS			
subjects affected / exposed	3 / 2061 (0.15%)	2 / 2056 (0.10%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 2061 (0.05%)	4 / 2056 (0.19%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG-INDUCED LIVER INJURY			

subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GALLBLADDER OBSTRUCTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC FAILURE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC LESION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATOTOXICITY			
subjects affected / exposed	3 / 2061 (0.15%)	5 / 2056 (0.24%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	3 / 3	5 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	5 / 2061 (0.24%)	18 / 2056 (0.88%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	5 / 5	18 / 19	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTRANSAMINASAEMIA			

subjects affected / exposed	74 / 2061 (3.59%)	86 / 2056 (4.18%)	11 / 2076 (0.53%)
occurrences causally related to treatment / all	95 / 98	101 / 104	6 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JAUNDICE			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ERYTHEMA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACNE			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGIODERMATITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANGIOEDEMA			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CUTANEOUS VASCULITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH			

subjects affected / exposed	4 / 2061 (0.19%)	7 / 2056 (0.34%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	4 / 4	7 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PRURITUS			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN NECROSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN SWELLING			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN ULCER			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHOTOSENSITIVITY REACTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAIL DISORDER			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTROPHIC SCAR			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EXFOLIATIVE RASH			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXIC EPIDERMAL NECROLYSIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URTICARIA			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CALCULUS URINARY			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHRITIC SYNDROME			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEPHROLITHIASIS			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL COLIC			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL FAILURE			
subjects affected / exposed	1 / 2061 (0.05%)	2 / 2056 (0.10%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY BLADDER HAEMORRHAGE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URETHRAL OBSTRUCTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERPARATHYROIDISM			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GOITRE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AUTOIMMUNE THYROIDITIS			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	4 / 2061 (0.19%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYALGIA			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST WALL NECROSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COSTOCHONDRITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUMBAR SPINAL STENOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE PAIN			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOSITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOARTHRITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOPOROSIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCLERODERMA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVIAL CYST			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNOVITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONDYLOLISTHESIS			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL WALL ABSCESS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABSCESS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE HEPATITIS B			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE SINUSITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
AMOEBIC DYSENTERY			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANTIBIOTIC ASSOCIATED COLITIS			

subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATYPICAL PNEUMONIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL ABSCESS			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BREAST CELLULITIS			
subjects affected / exposed	1 / 2061 (0.05%)	3 / 2056 (0.15%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS VIRAL			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATHETER SITE CELLULITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			

subjects affected / exposed	15 / 2061 (0.73%)	7 / 2056 (0.34%)	5 / 2076 (0.24%)
occurrences causally related to treatment / all	5 / 16	1 / 7	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	8 / 2061 (0.39%)	4 / 2056 (0.19%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	1 / 8	1 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHLAMYDIAL INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONJUNCTIVITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYSTITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST WALL ABSCESS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA INFECTIOUS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	6 / 2061 (0.29%)	4 / 2056 (0.19%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	2 / 6	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	3 / 2061 (0.15%)	3 / 2056 (0.15%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 3	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1N1 INFLUENZA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS B			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS C			

subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
DEVICE RELATED SEPSIS			
subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS VIRAL			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	1 / 2061 (0.05%)	3 / 2056 (0.15%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPLANT SITE CELLULITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTED CYST			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTED LYMPHOCELE			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOCALISED INFECTION			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISCITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE INFECTION			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARYNGITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTION			
subjects affected / exposed	2 / 2061 (0.10%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 2061 (0.15%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	1 / 3	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPH GLAND INFECTION			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPH NODE ABSCESS			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHANGITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALARIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS VIRAL			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAIL INFECTION			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROBORRELIOSIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MASTITIS			

subjects affected / exposed	2 / 2061 (0.10%)	6 / 2056 (0.29%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL CANDIDIASIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OTITIS MEDIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN ABSCESS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	14 / 2061 (0.68%)	9 / 2056 (0.44%)	10 / 2076 (0.48%)
occurrences causally related to treatment / all	8 / 14	2 / 9	4 / 11
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
PARONYCHIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA CYTOMEGALOVIRAL			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			

subjects affected / exposed	2 / 2061 (0.10%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	2 / 2061 (0.10%)	2 / 2056 (0.10%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	2 / 2056 (0.10%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	1 / 2061 (0.05%)	5 / 2056 (0.24%)	5 / 2076 (0.24%)
occurrences causally related to treatment / all	0 / 1	3 / 5	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
SIALOADENITIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUSITIS			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	2 / 2076 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TUBERCULOUS PLEURISY			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOFT TISSUE INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TUBERCULOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STREPTOCOCCAL SEPSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERINFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTH INFECTION			

subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STREPTOCOCCAL INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 2061 (0.10%)	2 / 2056 (0.10%)	7 / 2076 (0.34%)
occurrences causally related to treatment / all	1 / 2	0 / 2	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION BACTERIAL			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			

subjects affected / exposed	11 / 2061 (0.53%)	12 / 2056 (0.58%)	4 / 2076 (0.19%)
occurrences causally related to treatment / all	11 / 11	11 / 13	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DECREASED APPETITE			
subjects affected / exposed	3 / 2061 (0.15%)	3 / 2056 (0.15%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	3 / 3	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES MELLITUS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERNATRAEMIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERPHOSPHATASAEMIA			
subjects affected / exposed	4 / 2061 (0.19%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	3 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHAGIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOCALCAEMIA			

subjects affected / exposed	2 / 2061 (0.10%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	8 / 2061 (0.39%)	9 / 2056 (0.44%)	3 / 2076 (0.14%)
occurrences causally related to treatment / all	9 / 9	7 / 9	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 2061 (0.05%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	1 / 2056 (0.05%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
HYPERURICAEMIA			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	0 / 2076 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOVOLAEMIA			
subjects affected / exposed	1 / 2061 (0.05%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 2061 (0.00%)	0 / 2056 (0.00%)	1 / 2076 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Trastuzumab followed by Lapatinib		

Total subjects affected by serious adverse events			
subjects affected / exposed	299 / 2076 (14.40%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ACUTE LYMPHOCYTIC LEUKAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ACUTE PROMYELOCYTIC LEUKAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL CARCINOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL STROMAL TUMOUR			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HAEMANGIOMA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BENIGN BREAST NEOPLASM			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

BENIGN OVARIAN TUMOUR			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRIC CANCER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BORDERLINE OVARIAN TUMOUR			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BREAST CANCER			
subjects affected / exposed	3 / 2076 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
BREAST CANCER IN SITU			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COLON CANCER			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ENDOMETRIAL ADENOCARCINOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLADDER NEOPLASM			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INTRADUCTAL PAPILLOMA OF BREAST			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LEIOMYOMA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LEIOMYOSARCOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MENINGIOMA BENIGN			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LIPOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MALIGNANT MELANOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MENINGIOMA			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LENTIGO MALIGNA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
METASTASES TO CENTRAL NERVOUS SYSTEM			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NEUROENDOCRINE TUMOUR			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OVARIAN ADENOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OVARIAN CANCER			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OVARIAN GERM CELL TERATOMA BENIGN			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RECTAL CANCER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PANCREATIC CARCINOMA			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PAPILLARY THYROID CANCER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PARATHYROID TUMOUR BENIGN			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PLASMA CELL MYELOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OVARIAN NEOPLASM			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
SMALL CELL LUNG CANCER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SQUAMOUS CELL CARCINOMA OF THE VULVA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUPERFICIAL SPREADING MELANOMA STAGE UNSPECIFIED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
THYROID CANCER			

subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRANSITIONAL CELL CARCINOMA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UTERINE CANCER				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UTERINE LEIOMYOMA				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
HYPERTENSION				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
HYPOTENSION				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
JUGULAR VEIN THROMBOSIS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPERTENSIVE CRISIS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CIRCULATORY COLLAPSE				

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DEEP VEIN THROMBOSIS				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
EMBOLISM VENOUS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FLUSHING				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VENOUS THROMBOSIS LIMB				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VASCULAR INSUFFICIENCY				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
THROMBOSIS				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
SUPERFICIAL VEIN THROMBOSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBCLAVIAN VEIN THROMBOSIS				

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RHEUMATOID VASCULITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ORTHOSTATIC HYPOTENSION				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
ADVERSE DRUG REACTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ASTHENIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CHEST PAIN				
subjects affected / exposed	4 / 2076 (0.19%)			
occurrences causally related to treatment / all	4 / 5			
deaths causally related to treatment / all	0 / 0			
CHILLS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHRONIC FATIGUE SYNDROME				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DEATH				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GRANULOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FAT NECROSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FATIGUE			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
FEELING COLD			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DEVICE RELATED THROMBOSIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
IMPAIRED HEALING			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
IMPLANT SITE THROMBOSIS			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INFLAMMATION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LIPOGRANULOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MALAISE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NECROSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OEDEMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OEDEMA PERIPHERAL			

subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
MUCOSAL INFLAMMATION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PYREXIA				
subjects affected / exposed	16 / 2076 (0.77%)			
occurrences causally related to treatment / all	8 / 17			
deaths causally related to treatment / all	0 / 0			
SUDDEN DEATH				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Immune system disorders				
SARCOIDOSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANAPHYLACTIC REACTION				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
ANAPHYLACTOID REACTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DRUG HYPERSENSITIVITY				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPERSENSITIVITY				

subjects affected / exposed	4 / 2076 (0.19%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
BREAST HAEMATOMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ADENOMYOSIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BREAST CALCIFICATIONS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BREAST DISORDER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BREAST FIBROSIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BREAST INFLAMMATION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BREAST NECROSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BREAST SWELLING			

subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ENDOMETRIAL HYPERPLASIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UTERINE POLYP				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OVARIAN CYST				
subjects affected / exposed	4 / 2076 (0.19%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
OVARIAN CYST RUPTURED				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PELVIC PAIN				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
POSTMENOPAUSAL HAEMORRHAGE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INTERMENSTRUAL BLEEDING				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VAGINAL HAEMORRHAGE				

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
ACUTE RESPIRATORY DISTRESS SYNDROME				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
ATELECTASIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRONCHIECTASIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRONCHOSPASM				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HAEMOPTYSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DYSPHONIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DYSPNOEA				
subjects affected / exposed	3 / 2076 (0.14%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
DYSPNOEA EXERTIONAL				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
EPISTAXIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COUGH			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOXIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
LARYNGEAL OEDEMA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LUNG CONSOLIDATION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LUNG DISORDER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PNEUMOTHORAX			

subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PLEURAL EFFUSION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PLEURISY				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PLEURITIC PAIN				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONITIS				
subjects affected / exposed	4 / 2076 (0.19%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
LUNG INFILTRATION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PULMONARY EMBOLISM				
subjects affected / exposed	4 / 2076 (0.19%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
PULMONARY GRANULOMA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PULMONARY MASS				

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PULMONARY OEDEMA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PULMONARY THROMBOSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY FAILURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
RESTLESSNESS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SCHIZOPHRENIA				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SUICIDE ATTEMPT				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ABNORMAL BEHAVIOUR				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MENTAL DISORDER				

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COMPLETED SUICIDE				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
DEPRESSION				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
INSOMNIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MAJOR DEPRESSION				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ALCOHOL WITHDRAWAL SYNDROME				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Product issues				
THROMBOSIS IN DEVICE				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DEVICE DISLOCATION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DEVICE EXPULSION				

subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
AMYLASE INCREASED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BLOOD MAGNESIUM DECREASED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLOOD POTASSIUM DECREASED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLOOD UREA INCREASED			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ELECTROCARDIOGRAM ST SEGMENT DEPRESSION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COAGULATION TEST ABNORMAL			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
EASTERN COOPERATIVE ONCOLOGY GROUP PERFORMANCE STATUS WORSENED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ELECTROCARDIOGRAM ABNORMAL			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

BODY TEMPERATURE INCREASED				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ELECTROCARDIOGRAM T WAVE INVERSION				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
GAMMA-GLUTAMYLTRANSFERASE INCREASED				
subjects affected / exposed	4 / 2076 (0.19%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
INTERNATIONAL NORMALISED RATIO INCREASED				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LIPASE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LIVER FUNCTION TEST INCREASED				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PLATELET COUNT DECREASED				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
WEIGHT DECREASED				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

LIPASE INCREASED				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
CONTUSION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ALCOHOL POISONING				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANKLE FRACTURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CARBON MONOXIDE POISONING				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
CONCUSSION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FIBULA FRACTURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FOOT FRACTURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

FOREIGN BODY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FRACTURE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FRACTURED COCCYX			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LOWER LIMB FRACTURE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HUMERUS FRACTURE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
LIGAMENT INJURY			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HIP FRACTURE			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MULTIPLE INJURIES			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PELVIC FRACTURE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RADIATION FIBROSIS - LUNG			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RADIATION PNEUMONITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RADIATION SKIN INJURY			
subjects affected / exposed	3 / 2076 (0.14%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
RADIUS FRACTURE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RIB FRACTURE			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
ROAD TRAFFIC ACCIDENT			

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SEROMA				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
SPINAL COMPRESSION FRACTURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SPINAL FRACTURE				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STERNAL FRACTURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBDURAL HAEMORRHAGE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
THERMAL BURN				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
TIBIA FRACTURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UPPER LIMB FRACTURE				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
WRIST FRACTURE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
WOUND COMPLICATION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
GILBERT'S SYNDROME			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
CARDIAC ARREST			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ATRIAL THROMBOSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

ATRIAL TACHYCARDIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
ATRIAL FIBRILLATION			
subjects affected / exposed	4 / 2076 (0.19%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
ARRHYTHMIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ANGINA PECTORIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	6 / 2076 (0.29%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
ACUTE CORONARY SYNDROME			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LEFT VENTRICULAR DYSFUNCTION			

subjects affected / exposed	5 / 2076 (0.24%)		
occurrences causally related to treatment / all	4 / 5		
deaths causally related to treatment / all	0 / 0		
INTRACARDIAC THROMBUS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CARDIOMYOPATHY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CARDIAC VENTRICULAR THROMBOSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
PERICARDITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PERICARDIAL EFFUSION			

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PALPITATIONS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VENTRICULAR ARRHYTHMIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VENTRICULAR EXTRASYSTOLES				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VENTRICULAR TACHYCARDIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
AMYOTROPHIC LATERAL SCLEROSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BRAIN HYPOXIA				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
CEREBELLAR ATAXIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CEREBROVASCULAR ACCIDENT				

subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DIZZINESS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
EPILEPSY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FACIAL PARALYSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HEADACHE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOTONIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MIGRAINE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MOTOR NEURONE DISEASE			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NEUROPATHY PERIPHERAL			
subjects affected / exposed	4 / 2076 (0.19%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INTRACRANIAL ANEURYSM			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
POLYNEUROPATHY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
QUADRIPARESIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEIZURE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SEROTONIN SYNDROME			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SOMNOLENCE			

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SYNCOPE				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRANSIENT GLOBAL AMNESIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBARACHNOID HAEMORRHAGE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
LEUKOPENIA				
subjects affected / exposed	4 / 2076 (0.19%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
THROMBOCYTOPENIA				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PANCYTOPENIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NEUTROPENIA				
subjects affected / exposed	21 / 2076 (1.01%)			
occurrences causally related to treatment / all	25 / 25			
deaths causally related to treatment / all	0 / 0			
IRON DEFICIENCY ANAEMIA				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ANAEMIA			
subjects affected / exposed	6 / 2076 (0.29%)		
occurrences causally related to treatment / all	7 / 7		
deaths causally related to treatment / all	0 / 0		
EOSINOPHILIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
FEBRILE NEUTROPENIA			
subjects affected / exposed	6 / 2076 (0.29%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
AGRANULOCYTOSIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
VERTIGO POSITIONAL			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VERTIGO			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
TINNITUS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

DIPLOPIA				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RETINAL DETACHMENT				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PERIORBITAL OEDEMA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
ABDOMINAL PAIN LOWER				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ABDOMINAL PAIN UPPER				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANAL FISSURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANAL HAEMORRHAGE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COLITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ABDOMINAL MASS				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
ABDOMINAL PAIN			
subjects affected / exposed	4 / 2076 (0.19%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CONSTIPATION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIARRHOEA			
subjects affected / exposed	6 / 2076 (0.29%)		
occurrences causally related to treatment / all	5 / 6		
deaths causally related to treatment / all	0 / 0		
DUODENAL ULCER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DYSPEPSIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DYSPHAGIA			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ENTERITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ENTEROCOLITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
EPIPLOIC APPENDAGITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRIC HAEMORRHAGE			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
GASTRIC ULCER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRITIS			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL OBSTRUCTION			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL PERFORATION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL TOXICITY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL ULCER			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LOWER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ILEUS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LARGE INTESTINE PERFORATION			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HAEMORRHOIDS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NAUSEA			
subjects affected / exposed	3 / 2076 (0.14%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
OESOPHAGITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
REFLUX GASTRITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
STOMATITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
UPPER GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
VOLVULUS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VOMITING				
subjects affected / exposed	3 / 2076 (0.14%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
SMALL INTESTINAL OBSTRUCTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
BILE DUCT STENOSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BILIARY COLIC				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
CHOLECYSTITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HEPATIC FUNCTION ABNORMAL				
subjects affected / exposed	4 / 2076 (0.19%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
CHOLELITHIASIS				

subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GALLBLADDER OBSTRUCTION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEPATIC FAILURE			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HEPATIC LESION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HEPATITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HEPATOTOXICITY			
subjects affected / exposed	3 / 2076 (0.14%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
HYPERBILIRUBINAEMIA			

subjects affected / exposed	12 / 2076 (0.58%)			
occurrences causally related to treatment / all	12 / 12			
deaths causally related to treatment / all	0 / 0			
HYPERTRANSAMINASAEMIA				
subjects affected / exposed	55 / 2076 (2.65%)			
occurrences causally related to treatment / all	67 / 74			
deaths causally related to treatment / all	0 / 0			
JAUNDICE				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
ERYTHEMA				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
ACNE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANGIODERMATITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANGIOEDEMA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CUTANEOUS VASCULITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DERMATITIS ACNEIFORM				

subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
RASH			
subjects affected / exposed	4 / 2076 (0.19%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
PRURITUS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SKIN NECROSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SKIN SWELLING			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SKIN ULCER			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PHOTOSENSITIVITY REACTION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NAIL DISORDER				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPERTROPHIC SCAR				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
EXFOLIATIVE RASH				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TOXIC EPIDERMAL NECROLYSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URTICARIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
ACUTE KIDNEY INJURY				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CALCULUS URINARY				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NEPHRITIC SYNDROME				

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
NEPHROLITHIASIS				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
RENAL COLIC				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RENAL FAILURE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URINARY BLADDER HAEMORRHAGE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URETHRAL OBSTRUCTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
HYPOTHYROIDISM				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HYPERPARATHYROIDISM				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GOITRE				

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
AUTOIMMUNE THYROIDITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
ARTHRALGIA				
subjects affected / exposed	3 / 2076 (0.14%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
BACK PAIN				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MYALGIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CHEST WALL NECROSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COSTOCHONDRITIS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LUMBAR SPINAL STENOSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
MUSCULOSKELETAL CHEST PAIN				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BONE PAIN			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MYOSITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OSTEOARTHRITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OSTEOPOROSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SCLERODERMA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
SYNOVIAL CYST			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SYNOVITIS			

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SPONDYLOLISTHESIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
ABDOMINAL WALL ABSCESS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ABSCESS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ACUTE HEPATITIS B				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ACUTE SINUSITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
AMOEBIC DYSENTERY				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
BACTERIAL INFECTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ANAL INFECTION				

subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ANTIBIOTIC ASSOCIATED COLITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ATYPICAL PNEUMONIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BACTERAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ANAL ABSCESS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BREAST CELLULITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BRONCHITIS			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
BRONCHITIS VIRAL			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CATHETER SITE CELLULITIS			

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CELLULITIS				
subjects affected / exposed	14 / 2076 (0.67%)			
occurrences causally related to treatment / all	10 / 17			
deaths causally related to treatment / all	0 / 0			
DEVICE RELATED INFECTION				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
CHLAMYDIAL INFECTION				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CLOSTRIDIUM DIFFICILE INFECTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CONJUNCTIVITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CYSTITIS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CHEST WALL ABSCESS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
DIARRHOEA INFECTIOUS				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIVERTICULITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
ERYSIPELAS			
subjects affected / exposed	4 / 2076 (0.19%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
GASTRIC INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS			
subjects affected / exposed	3 / 2076 (0.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
H1N1 INFLUENZA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HEPATITIS B			

subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
HEPATITIS C				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
DEVICE RELATED SEPSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HEPATITIS VIRAL				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HERPES ZOSTER				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
IMPLANT SITE CELLULITIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFECTED CYST				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INFECTED LYMPHOCELE				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
LOCALISED INFECTION				

subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INFLUENZA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INTERVERTEBRAL DISCITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LARGE INTESTINE INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LARYNGITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
INFECTION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
LYMPH GLAND INFECTION			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LYMPH NODE ABSCESS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LYMPHANGITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MALARIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NEUTROPENIC SEPSIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
MENINGITIS VIRAL			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NAIL INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NASOPHARYNGITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NEUROBORRELIOSIS			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MASTITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OESOPHAGEAL CANDIDIASIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OESOPHAGEAL INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OSTEOMYELITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OTITIS MEDIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
OVARIAN ABSCESS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PERITONITIS			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PHARYNGITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PNEUMOCYSTIS JIROVECII INFECTION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA			
subjects affected / exposed	11 / 2076 (0.53%)		
occurrences causally related to treatment / all	2 / 12		
deaths causally related to treatment / all	0 / 0		
PARONYCHIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA CYTOMEGALOVIRAL			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYELONEPHRITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SKIN INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
SEPSIS			
subjects affected / exposed	3 / 2076 (0.14%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
SIALOADENITIS			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SINUSITIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
TUBERCULOUS PLEURISY			

subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SOFT TISSUE INFECTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
STAPHYLOCOCCAL BACTERAEMIA				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
STAPHYLOCOCCAL INFECTION				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
TUBERCULOSIS				
subjects affected / exposed	1 / 2076 (0.05%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
STREPTOCOCCAL SEPSIS				
subjects affected / exposed	0 / 2076 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SUBCUTANEOUS ABSCESS				
subjects affected / exposed	2 / 2076 (0.10%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
SUPERINFECTION				

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
TOOTH INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
STREPTOCOCCAL INFECTION			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
UPPER RESPIRATORY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT INFECTION			
subjects affected / exposed	6 / 2076 (0.29%)		
occurrences causally related to treatment / all	4 / 7		
deaths causally related to treatment / all	0 / 0		
UROSEPSIS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VIRAL INFECTION			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
WOUND INFECTION			
subjects affected / exposed	2 / 2076 (0.10%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
WOUND INFECTION BACTERIAL			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	3 / 2076 (0.14%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
DECREASED APPETITE			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIABETES MELLITUS			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPERCHOLESTEROLAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HYPERNATRAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPERPHOSPHATASAEMIA			
subjects affected / exposed	4 / 2076 (0.19%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
HYPOPHAGIA			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOCALCAEMIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOKALAEMIA			
subjects affected / exposed	1 / 2076 (0.05%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPONATRAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPERURICAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOVOLAEMIA			
subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
METABOLIC ACIDOSIS			

subjects affected / exposed	0 / 2076 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lapatinib plus Trastuzumab	Lapatinib	Trastuzumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1930 / 2061 (93.64%)	1887 / 2056 (91.78%)	1649 / 2076 (79.43%)
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	211 / 2061 (10.24%)	190 / 2056 (9.24%)	272 / 2076 (13.10%)
occurrences (all)	232	199	294
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	227 / 2061 (11.01%)	132 / 2056 (6.42%)	171 / 2076 (8.24%)
occurrences (all)	270	158	208
OEDEMA PERIPHERAL			
subjects affected / exposed	144 / 2061 (6.99%)	138 / 2056 (6.71%)	160 / 2076 (7.71%)
occurrences (all)	158	153	184
MUCOSAL INFLAMMATION			
subjects affected / exposed	227 / 2061 (11.01%)	164 / 2056 (7.98%)	114 / 2076 (5.49%)
occurrences (all)	265	193	126
FATIGUE			
subjects affected / exposed	511 / 2061 (24.79%)	443 / 2056 (21.55%)	439 / 2076 (21.15%)
occurrences (all)	603	502	550
ASTHENIA			
subjects affected / exposed	202 / 2061 (9.80%)	175 / 2056 (8.51%)	171 / 2076 (8.24%)
occurrences (all)	259	208	213
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	219 / 2061 (10.63%)	153 / 2056 (7.44%)	242 / 2076 (11.66%)
occurrences (all)	252	173	282
DYSPNOEA			

subjects affected / exposed	147 / 2061 (7.13%)	103 / 2056 (5.01%)	170 / 2076 (8.19%)
occurrences (all)	151	106	202
EPISTAXIS			
subjects affected / exposed	319 / 2061 (15.48%)	244 / 2056 (11.87%)	165 / 2076 (7.95%)
occurrences (all)	363	268	179
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	168 / 2061 (8.15%)	152 / 2056 (7.39%)	190 / 2076 (9.15%)
occurrences (all)	182	163	220
Injury, poisoning and procedural complications			
RADIATION SKIN INJURY			
subjects affected / exposed	91 / 2061 (4.42%)	82 / 2056 (3.99%)	129 / 2076 (6.21%)
occurrences (all)	92	82	132
Cardiac disorders			
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	59 / 2061 (2.86%)	45 / 2056 (2.19%)	107 / 2076 (5.15%)
occurrences (all)	65	49	115
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	104 / 2061 (5.05%)	115 / 2056 (5.59%)	118 / 2076 (5.68%)
occurrences (all)	111	122	130
HEADACHE			
subjects affected / exposed	192 / 2061 (9.32%)	161 / 2056 (7.83%)	262 / 2076 (12.62%)
occurrences (all)	227	193	314
NEUROPATHY PERIPHERAL			
subjects affected / exposed	177 / 2061 (8.59%)	173 / 2056 (8.41%)	178 / 2076 (8.57%)
occurrences (all)	189	185	197
PARAESTHESIA			
subjects affected / exposed	125 / 2061 (6.07%)	107 / 2056 (5.20%)	131 / 2076 (6.31%)
occurrences (all)	141	114	181
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	164 / 2061 (7.96%)	162 / 2056 (7.88%)	194 / 2076 (9.34%)
occurrences (all)	201	175	232
Blood and lymphatic system disorders			
LEUKOPENIA			

subjects affected / exposed	174 / 2061 (8.44%)	155 / 2056 (7.54%)	168 / 2076 (8.09%)
occurrences (all)	300	268	295
ANAEMIA			
subjects affected / exposed	226 / 2061 (10.97%)	169 / 2056 (8.22%)	223 / 2076 (10.74%)
occurrences (all)	255	184	253
NEUTROPENIA			
subjects affected / exposed	233 / 2061 (11.31%)	220 / 2056 (10.70%)	179 / 2076 (8.62%)
occurrences (all)	396	365	292
Gastrointestinal disorders			
STOMATITIS			
subjects affected / exposed	203 / 2061 (9.85%)	161 / 2056 (7.83%)	98 / 2076 (4.72%)
occurrences (all)	249	185	114
NAUSEA			
subjects affected / exposed	393 / 2061 (19.07%)	381 / 2056 (18.53%)	285 / 2076 (13.73%)
occurrences (all)	504	471	387
DYSPEPSIA			
subjects affected / exposed	174 / 2061 (8.44%)	156 / 2056 (7.59%)	116 / 2076 (5.59%)
occurrences (all)	181	173	124
CONSTIPATION			
subjects affected / exposed	120 / 2061 (5.82%)	135 / 2056 (6.57%)	156 / 2076 (7.51%)
occurrences (all)	132	143	194
ABDOMINAL PAIN UPPER			
subjects affected / exposed	137 / 2061 (6.65%)	110 / 2056 (5.35%)	78 / 2076 (3.76%)
occurrences (all)	160	119	86
ABDOMINAL PAIN			
subjects affected / exposed	146 / 2061 (7.08%)	148 / 2056 (7.20%)	79 / 2076 (3.81%)
occurrences (all)	164	164	101
DIARRHOEA			
subjects affected / exposed	1516 / 2061 (73.56%)	1278 / 2056 (62.16%)	399 / 2076 (19.22%)
occurrences (all)	2752	1973	527
VOMITING			
subjects affected / exposed	251 / 2061 (12.18%)	215 / 2056 (10.46%)	151 / 2076 (7.27%)
occurrences (all)	334	278	180
Hepatobiliary disorders			

HYPERTRANSAMINASAEMIA			
subjects affected / exposed	348 / 2061 (16.89%)	366 / 2056 (17.80%)	281 / 2076 (13.54%)
occurrences (all)	600	657	482
HYPERBILIRUBINAEMIA			
subjects affected / exposed	96 / 2061 (4.66%)	121 / 2056 (5.89%)	31 / 2076 (1.49%)
occurrences (all)	133	165	39
Skin and subcutaneous tissue disorders			
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	181 / 2061 (8.78%)	126 / 2056 (6.13%)	47 / 2076 (2.26%)
occurrences (all)	197	130	50
PRURITUS			
subjects affected / exposed	316 / 2061 (15.33%)	334 / 2056 (16.25%)	134 / 2076 (6.45%)
occurrences (all)	380	382	145
ACNE			
subjects affected / exposed	134 / 2061 (6.50%)	112 / 2056 (5.45%)	20 / 2076 (0.96%)
occurrences (all)	149	123	21
ALOPECIA			
subjects affected / exposed	109 / 2061 (5.29%)	110 / 2056 (5.35%)	151 / 2076 (7.27%)
occurrences (all)	109	111	152
DERMATITIS ACNEIFORM			
subjects affected / exposed	117 / 2061 (5.68%)	124 / 2056 (6.03%)	19 / 2076 (0.92%)
occurrences (all)	138	146	24
DRY SKIN			
subjects affected / exposed	262 / 2061 (12.71%)	280 / 2056 (13.62%)	86 / 2076 (4.14%)
occurrences (all)	282	305	92
ERYTHEMA			
subjects affected / exposed	122 / 2061 (5.92%)	93 / 2056 (4.52%)	87 / 2076 (4.19%)
occurrences (all)	149	112	99
NAIL DISORDER			
subjects affected / exposed	359 / 2061 (17.42%)	294 / 2056 (14.30%)	220 / 2076 (10.60%)
occurrences (all)	384	312	231
RASH			
subjects affected / exposed	771 / 2061 (37.41%)	767 / 2056 (37.31%)	223 / 2076 (10.74%)
occurrences (all)	1010	959	265
SKIN FISSURES			

subjects affected / exposed	145 / 2061 (7.04%)	123 / 2056 (5.98%)	7 / 2076 (0.34%)
occurrences (all)	165	139	8
Musculoskeletal and connective tissue disorders			
MYALGIA			
subjects affected / exposed	211 / 2061 (10.24%)	174 / 2056 (8.46%)	252 / 2076 (12.14%)
occurrences (all)	274	231	368
BONE PAIN			
subjects affected / exposed	87 / 2061 (4.22%)	91 / 2056 (4.43%)	122 / 2076 (5.88%)
occurrences (all)	103	107	146
BACK PAIN			
subjects affected / exposed	128 / 2061 (6.21%)	119 / 2056 (5.79%)	126 / 2076 (6.07%)
occurrences (all)	138	124	133
ARTHRALGIA			
subjects affected / exposed	340 / 2061 (16.50%)	320 / 2056 (15.56%)	451 / 2076 (21.72%)
occurrences (all)	404	366	559
PAIN IN EXTREMITY			
subjects affected / exposed	135 / 2061 (6.55%)	98 / 2056 (4.77%)	175 / 2076 (8.43%)
occurrences (all)	154	109	216
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	117 / 2061 (5.68%)	93 / 2056 (4.52%)	118 / 2076 (5.68%)
occurrences (all)	144	107	149
PARONYCHIA			
subjects affected / exposed	262 / 2061 (12.71%)	206 / 2056 (10.02%)	22 / 2076 (1.06%)
occurrences (all)	323	247	26
NASOPHARYNGITIS			
subjects affected / exposed	128 / 2061 (6.21%)	96 / 2056 (4.67%)	150 / 2076 (7.23%)
occurrences (all)	152	108	189
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	223 / 2061 (10.82%)	188 / 2056 (9.14%)	142 / 2076 (6.84%)
occurrences (all)	268	215	173
HYPERPHOSPHATASAEMIA			

subjects affected / exposed	81 / 2061 (3.93%)	120 / 2056 (5.84%)	76 / 2076 (3.66%)
occurrences (all)	95	127	87

Non-serious adverse events	Trastuzumab followed by Lapatinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1862 / 2076 (89.69%)		
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	225 / 2076 (10.84%)		
occurrences (all)	240		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	188 / 2076 (9.06%)		
occurrences (all)	222		
OEDEMA PERIPHERAL			
subjects affected / exposed	149 / 2076 (7.18%)		
occurrences (all)	174		
MUCOSAL INFLAMMATION			
subjects affected / exposed	149 / 2076 (7.18%)		
occurrences (all)	171		
FATIGUE			
subjects affected / exposed	515 / 2076 (24.81%)		
occurrences (all)	615		
ASTHENIA			
subjects affected / exposed	178 / 2076 (8.57%)		
occurrences (all)	218		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	201 / 2076 (9.68%)		
occurrences (all)	225		
DYSPNOEA			
subjects affected / exposed	146 / 2076 (7.03%)		
occurrences (all)	155		
EPISTAXIS			

subjects affected / exposed	213 / 2076 (10.26%)		
occurrences (all)	238		
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	172 / 2076 (8.29%)		
occurrences (all)	187		
Injury, poisoning and procedural complications			
RADIATION SKIN INJURY			
subjects affected / exposed	127 / 2076 (6.12%)		
occurrences (all)	129		
Cardiac disorders			
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	46 / 2076 (2.22%)		
occurrences (all)	52		
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	127 / 2076 (6.12%)		
occurrences (all)	138		
HEADACHE			
subjects affected / exposed	241 / 2076 (11.61%)		
occurrences (all)	295		
NEUROPATHY PERIPHERAL			
subjects affected / exposed	183 / 2076 (8.82%)		
occurrences (all)	192		
PARAESTHESIA			
subjects affected / exposed	110 / 2076 (5.30%)		
occurrences (all)	131		
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	159 / 2076 (7.66%)		
occurrences (all)	177		
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	138 / 2076 (6.65%)		
occurrences (all)	225		
ANAEMIA			

subjects affected / exposed	168 / 2076 (8.09%)		
occurrences (all)	186		
NEUTROPENIA			
subjects affected / exposed	175 / 2076 (8.43%)		
occurrences (all)	303		
Gastrointestinal disorders			
STOMATITIS			
subjects affected / exposed	141 / 2076 (6.79%)		
occurrences (all)	159		
NAUSEA			
subjects affected / exposed	393 / 2076 (18.93%)		
occurrences (all)	496		
DYSPEPSIA			
subjects affected / exposed	140 / 2076 (6.74%)		
occurrences (all)	151		
CONSTIPATION			
subjects affected / exposed	184 / 2076 (8.86%)		
occurrences (all)	211		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	111 / 2076 (5.35%)		
occurrences (all)	121		
ABDOMINAL PAIN			
subjects affected / exposed	108 / 2076 (5.20%)		
occurrences (all)	120		
DIARRHOEA			
subjects affected / exposed	1039 / 2076 (50.05%)		
occurrences (all)	1450		
VOMITING			
subjects affected / exposed	181 / 2076 (8.72%)		
occurrences (all)	220		
Hepatobiliary disorders			
HYPERTRANSAMINASAEMIA			
subjects affected / exposed	378 / 2076 (18.21%)		
occurrences (all)	637		
HYPERBILIRUBINAEMIA			

subjects affected / exposed	103 / 2076 (4.96%)		
occurrences (all)	133		
Skin and subcutaneous tissue disorders			
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	105 / 2076 (5.06%)		
occurrences (all)	111		
PRURITUS			
subjects affected / exposed	268 / 2076 (12.91%)		
occurrences (all)	304		
ACNE			
subjects affected / exposed	138 / 2076 (6.65%)		
occurrences (all)	144		
ALOPECIA			
subjects affected / exposed	135 / 2076 (6.50%)		
occurrences (all)	137		
DERMATITIS ACNEIFORM			
subjects affected / exposed	96 / 2076 (4.62%)		
occurrences (all)	106		
DRY SKIN			
subjects affected / exposed	244 / 2076 (11.75%)		
occurrences (all)	265		
ERYTHEMA			
subjects affected / exposed	104 / 2076 (5.01%)		
occurrences (all)	116		
NAIL DISORDER			
subjects affected / exposed	272 / 2076 (13.10%)		
occurrences (all)	285		
RASH			
subjects affected / exposed	685 / 2076 (33.00%)		
occurrences (all)	862		
SKIN FISSURES			
subjects affected / exposed	98 / 2076 (4.72%)		
occurrences (all)	103		
Musculoskeletal and connective tissue disorders			

MYALGIA			
subjects affected / exposed	214 / 2076 (10.31%)		
occurrences (all)	289		
BONE PAIN			
subjects affected / exposed	109 / 2076 (5.25%)		
occurrences (all)	130		
BACK PAIN			
subjects affected / exposed	133 / 2076 (6.41%)		
occurrences (all)	140		
ARTHRALGIA			
subjects affected / exposed	348 / 2076 (16.76%)		
occurrences (all)	415		
PAIN IN EXTREMITY			
subjects affected / exposed	125 / 2076 (6.02%)		
occurrences (all)	140		
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	96 / 2076 (4.62%)		
occurrences (all)	113		
PARONYCHIA			
subjects affected / exposed	165 / 2076 (7.95%)		
occurrences (all)	185		
NASOPHARYNGITIS			
subjects affected / exposed	111 / 2076 (5.35%)		
occurrences (all)	128		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	173 / 2076 (8.33%)		
occurrences (all)	189		
HYPERPHOSPHATASAEMIA			
subjects affected / exposed	109 / 2076 (5.25%)		
occurrences (all)	118		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 April 2008	Amendment No. 01: Implementation of additional monitoring of liver enzymes and associated criteria for study drug discontinuation, modification of the study inclusion/ exclusion criteria, provide clarification to the length of follow up, and permitted chemotherapy regimens. To provide clarification regarding the dosing of study therapy and the management of AEs.
14 August 2008	Amendment No. 02: Implementation of a lower starting dose of lapatinib (750 mg) during chemotherapy only in the Lap+Tras arm of Design 2 to diminish the chance of diarrhea occurrence. To allow patients randomized in the Tras-Lap arm of both designs to receive lapatinib after the occurrence of a secondary cardiac endpoint during trastuzumab administration only if LVEF after the washout period (6 weeks) and prior to lapatinib administration is ≥50%. To clarify the extent and nature of future translational research studies and provide revised timelines for circulating tumor cell collection.
12 February 2009	Amendment No. 03: Inclusion of statement indicating the possible accrual imbalance between Design 1 and Design 2 and possible future need to close screening to a design.
19 March 2009	Amendment No. 04: To allow the inclusion of docetaxel in Design 2, implement an additional interim analysis for analyses at 400, 700 and 1000 DFS events with final analysis after 1388 DFS events, and allow the use of Breast MRI scans instead of mammograms.
20 November 2009	Amendment No. 05: Inclusion of Design 2B and associated updates to enrollment (maximum sample size of 8400 patients) and revised timelines for circulating tumor cell collection.
27 January 2010	Amendment No. 06: Reduction of lapatinib dose when used concurrently with chemotherapy in the Lap arm and the Lap+Tras arm of Designs 2 and 2B to diminish the chance of diarrhea occurrence.
29 March 2010	Amendment No. 07: To clarify statistical plans for interim and final analyses, include the collection of a FFPE tumor block for future research, to update additional medicines added to the prohibited medications list for patients taking lapatinib.
02 August 2010	Amendment No. 08: To add a new statistical section entitled "Registration Strategy for ALTTO – June 2010", and thus support the modification of the analysis plan by the sponsor at the time (GSK). Inclusion of a statement clarifying that after completion of study treatment, patients enrolled in this study may receive anti-cancer therapy in other trials only if the trial has been approved by the Steering Committee. Clarification regarding the reporting of post-study treatment long-term AEs, Grade 4 neutropenia/leukopenia as an SAE, diarrhea management in lapatinib-containing arms, and the dose adjustments of trastuzumab and chemotherapy due to substantial weight changes and overweight/obese patients. Inclusion of the collection of a FNA sample will be allowed for certain patients.
28 October 2010	Amendment No. 09: Add NCI/CTEP recommendation for the calculation of the carboplatin dose and to add the maximum dose of carboplatin based on the target area under the curve (AUC) 6 is 900 mg.

17 October 2011	Amendment No. 10: To implement the recommendations by the ALTTO Steering Committee due to the IDMC meeting (August 18, 2011). Guidance for patient withdrawal from the study while allowing for collection of OS information, patients who were considered lost to follow-up, regarding prohibited medications and future trial medications. Clarification of diarrhea management, assessments beyond study treatment completion to determine secondary cardiac event, lobular carcinoma in situ and ductal carcinoma in situ reporting.
18 March 2016	Amendment No. 11: To update the assessment schedule, specify that after the patient completed the 10-year follow-up post randomization, only drug-related SAEs were to be reported, add the definition of EOS for clarity purposes, add details regarding explorative subgroup analyses of DFS for specific risk factors, allow broader use of the previously collected pharmacogenetic samples and the previously generated genetic data, and to implement changes in secondary endpoints.
05 July 2016	Amendment No. 12: To delete or replace references to GSK or its staff with that of Novartis and its authorized agents to align with the change of sponsorship, and to make administrative changes to align with study-specific processes and procedures. As the burden on patients was reduced by decreasing the number of procedures that required a physical visit to the site, the optional collection of samples at the time of relapse was also deleted.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com for complete trial results.

Notes: