Clinical trial results:
An Open-Label, Randomized, Multicenter Phase IIa Study Evaluating Pertuzumab in Combination with Trastuzumab and Chemotherapy in Patients with HER2-Positive Advanced Gastric Cancer

Summary

EudraCT number	2011-002331-25
Trial protocol	DE ES BE CZ NL IT
Global end of trial date	31 October 2017

Results information

Result version number	v1 (current)
This version publication date	16 November 2018
First version publication date	04 June 2016

Trial information

Trial identification

Sponsor protocol code	BP27836

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01461057
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To estimate the minimum (trough) serum pertuzumab concentration (Cmin) at Day 43 (pre-dose Cycle 3), for two dose levels of pertuzumab given every three weeks (Q3W) in order to identify a dose that produces a steady-state Cmin of greater than or equal to (>=) 20 microgram per millliter (mg/mL) in 90% of subjects receiving pertuzumab and trastuzumab plus chemotherapy as first-line treatment for human epidermal growth factor receptor 2 (HER2)-positive inoperable locally advanced or recurrent and/or metastatic adenocarcinoma of the stomach or gastroesophageal junction (GEJ).

- To evaluate the safety and tolerability of two dose levels of pertuzumab in combination with trastuzumab and chemotherapy administered every 3 weeks to subjects with HER2-positive inoperable locally advanced or recurrent and/or metastatic adenocarcinoma of the stomach or GEJ.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Spain: 4
Worldwide total number of subjects	30
EEA total number of subjects	13

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)	16
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 30 subjects were randomised in a 1:1 ratio to the two treatment arms. All subjects received study medication (any amount) and were evaluable for safety.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pertuzumab 840/420 mg

Arm description:

Subjects received pertuzumab as an intravenous (IV) infusion at a loading dose of 840 milligram (mg) for cycle 1 and a dose of 420 mg every three weeks (Q3W) for cycles 2-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 milligram per metre square (mg/m^2) was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 milligram per kilogram (mg/kg) for Cycle 1 and a dose of 6 mg/kg q3w for subsequent cycles.

Arm type	Experimental
Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	Herceptin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received trastuzumab as an IV infusion at a loading dose of 8 milligram per kilogram (mg/kg) on day 1 cycle 1 and dose of 6 mg/kg q3w for subsequent cycles until disease progression or unacceptable toxicity.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects recevied cisplatin 80 milligram per cubic metre (mg/m^3) as a 2 hour IV infusion on day 1 of each cycle.

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

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2 by mouth twice daily, from the evening of day 1 to the morning of day 15 of each cycle, for a total of six cycles or until investigator-assessed disease progression or unmanageable toxicity, whichever occurred first.

Investigational medicinal product name	Pertuzumab
Investigational medicinal product code	
Other name	Perjeta
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were administered pertuzumab as an IV infusion at a loading dose of 840 mg on day 1 cycle 1 and a dose of 420 mg for cycles 2-6.

Arm title	Pertuzumab 840/840 mg

Arm description:

Subjects received pertuzumab 840 mg as an IV infusion Q3W for cycles 1-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 mg/m^2 was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 mg/kg for Cycle 1 and a dose of 6 mg/kg q3w for subsequent cycles.

Arm type	Experimental
Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	Herceptin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received trastuzumab as an IV infusion at a loading dose of 8 mg/kg on day 1 cycle 1 and dose of 6 mg/kg q3w for subsequent cycles until disease progression or unacceptable toxicity.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects recevied cisplatin 80 mg/m^3 as a 2 hour IV infusion on day 1 of each cycle.

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

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2 by mouth twice daily, from the evening of day 1 to the morning of day 15 of each cycle, for a total of six cycles or until investigator-assessed disease progression or unmanageable toxicity, whichever occurred first.

Investigational medicinal product name	Pertuzumab
Investigational medicinal product code	
Other name	Perjeta
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were administered pertuzumab as an IV infusion at a loading dose of 840 mg on day 1 for cycles 1-6.

Number of subjects in period 1	Pertuzumab 840/420 mg	Pertuzumab 840/840 mg
Started	15	15
Completed	0	0
Not completed	15	15
Consent withdrawn by subject	2	3
Physician decision	-	2
Study terminated by Sponsor	2	-
Adverse event, non-fatal	-	1
Death	10	9
Progression of disease	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Pertuzumab 840/420 mg
Reporting group description:	
Subjects received pertuzumab as an intravenous (IV) infusion at a loading dose of 840 milligram (mg) for cycle 1 and a dose of 420 mg every three weeks (Q3W) for cycles 2-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 milligram per metre square (mg/m^2) was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 milligram per kilogram (mg/kg) for Cycle 1 and a dose of 6 mg/kg q3w for subsequent cycles.	
Reporting group title	Pertuzumab 840/840 mg
Reporting group description:	
Subjects received pertuzumab 840 mg as an IV infusion Q3W for cycles 1-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 mg/m^2 was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 mg/kg for Cycle 1 and a dose of 6 mg/kg q3w for subsequent cycles.	

Reporting group values	Pertuzumab 840/420 mg	Pertuzumab 840/840 mg	Total
Number of subjects	15	15	30
Age categorical Units: Subjects			
18 - 40 years	2	1	3
41 - 64 years	4	9	13
Greater than or equal to (>=) 65 years	9	5	14
Age continuous Units: years			
arithmetic mean	60.6	57.3	
standard deviation	± 14.7	± 11.5	-
Gender categorical Units: Subjects			
Female	1	5	6
Male	14	10	24

End points

End points reporting groups

Reporting group title	Pertuzumab 840/420 mg

Reporting group description:

Subjects received pertuzumab as an intravenous (IV) infusion at a loading dose of 840 milligram (mg) for cycle 1 and a dose of 420 mg every three weeks (Q3W) for cycles 2-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 milligram per metre square (mg/m^2) was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 milligram per kilogram (mg/kg) for Cycle 1 and a dose of 6 mg/kg q3w for subsequent cycles.

Reporting group title	Pertuzumab 840/840 mg

Reporting group description:

Subjects received pertuzumab 840 mg as an IV infusion Q3W for cycles 1-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 mg/m^2 was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 mg/kg for Cycle 1 and a dose of 6 mg/kg q3w for subsequent cycles.

Primary: Percentage of Subjects With Day 43 Serum Pertuzumab Trough Concentrations Greater Than or Equal to (>=) 20 microgram per millilitre (mcg/mL)

End point title	Percentage of Subjects With Day 43 Serum Pertuzumab Trough Concentrations Greater Than or Equal to (>=) 20 microgram per millilitre (mcg/mL)[1]

End point description:

The primary pharmacokinetic (PK) analysis population consisted of all subjects with a measurable PK samples on Day 43.

End point type	Primary

End point timeframe:

Day 43

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported.

End point values	Pertuzumab 840/420 mg	Pertuzumab 840/840 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	12		
Units: percentage of subjects				
number (confidence interval 95%)	91.6 (78.3 to 99.2)	98.3 (91.4 to 99.97)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events (AEs)

End point title	Number of Subjects With Adverse Events (AEs)[2]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a subject administered the investigational product which does not necessarily have a causal relationship with this treatment. Safety population included all subjects who were randomised and received at least one dose of study treatment.

End point type	Primary

End point timeframe:

From randomisation of first subject to end of study (approximately 6 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported.

End point values	Pertuzumab 840/420 mg	Pertuzumab 840/840 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: subjects	15	15		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation of first participant to end of study (approximately 6 years)

Adverse event reporting additional description:

An adverse event (AE) was defined as any untoward medical occurrence in a subject administered the investigational product which does not necessarily have a causal relationship with this treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Pertuzumab 840/840 mg

Reporting group description:

Subjects received pertuzumab 840 mg as an IV infusion Q3W for cycles 1-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 mg/m^2 was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 mg/kg for Cycle 1 and a dose of 6 mg/kg Q3W for subsequent cycles.

Reporting group title	Pertuzumab 840/420 mg

Reporting group description:

Subjects received pertuzumab as an intravenous (IV) infusion at a loading dose of 840 milligram (mg) for cycle 1 and a dose of 420 mg every three weeks (Q3W) for cycles 2-6. Subjects in both arms received trastuzumab, cisplatin, and capecitabine. Capecitabine 1000 milligram per metre square (mg/m^2) was administered orally twice daily, from the evening of Day 1 to the morning of Day 15 of each cycle. Cisplatin 80 mg/m^2 was administered as an IV infusion on Day 1 of each cycle. Trastuzumab was administered at a loading dose of 8 milligram per kilogram (mg/kg) for Cycle 1 and a dose of 6 mg/kg Q3W for subsequent cycles.

Serious adverse events	Pertuzumab 840/840 mg	Pertuzumab 840/420 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 15 (66.67%)	11 / 15 (73.33%)	
number of deaths (all causes)	9	10	
number of deaths resulting from adverse events	1	0	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myoglobin blood increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutrophil count decreased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 15 (0.00%)	4 / 15 (26.67%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ascites			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 15 (20.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Biliary sepsis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Herpes zoster			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food intolerance			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pertuzumab 840/840 mg	Pertuzumab 840/420 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	15 / 15 (100.00%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Embolism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Flushing			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	5	
Hypertensive crisis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Subclavian vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	3 / 15 (20.00%)	6 / 15 (40.00%)	
occurrences (all)	4	6	
Catheter site pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Chest pain			

subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Chills			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
occurrences (all)	1	3	
Face oedema			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Fatigue			
subjects affected / exposed	7 / 15 (46.67%)	5 / 15 (33.33%)	
occurrences (all)	16	18	
General physical health deterioration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Injection site reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	2 / 15 (13.33%)	4 / 15 (26.67%)	
occurrences (all)	3	6	
Oedema peripheral			
subjects affected / exposed	4 / 15 (26.67%)	5 / 15 (33.33%)	
occurrences (all)	5	7	
Pain			
subjects affected / exposed	3 / 15 (20.00%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Pyrexia			
subjects affected / exposed	2 / 15 (13.33%)	6 / 15 (40.00%)	
occurrences (all)	4	8	
Xerosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			

Drug hypersensitivity			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 15 (20.00%)	4 / 15 (26.67%)	
occurrences (all)	3	6	
Dyspnoea			
subjects affected / exposed	3 / 15 (20.00%)	2 / 15 (13.33%)	
occurrences (all)	3	2	
Dyspnoea exertional			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Hiccups			
subjects affected / exposed	0 / 15 (0.00%)	5 / 15 (33.33%)	
occurrences (all)	0	7	
Oropharyngeal pain			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	1 / 15 (6.67%)	6 / 15 (40.00%)	
occurrences (all)	1	8	
Rales			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Rhinorrhoea			

subjects affected / exposed	4 / 15 (26.67%)	3 / 15 (20.00%)	
occurrences (all)	4	3	
Nasal inflammation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Affective disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Insomnia			
subjects affected / exposed	2 / 15 (13.33%)	4 / 15 (26.67%)	
occurrences (all)	2	4	
Sleep disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Somatic symptom disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	3	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Alanine aminotransferase increased			
subjects affected / exposed	3 / 15 (20.00%)	2 / 15 (13.33%)	
occurrences (all)	3	3	
Amylase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	
occurrences (all)	3	2	
Bilirubin conjugated increased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Blood cholesterol increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood cholinesterase decreased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Blood creatine phosphokinase MB increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood fibrinogen increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood iron increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood potassium increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood urea increased			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 15 (6.67%)	4 / 15 (26.67%)	
occurrences (all)	1	4	
Ejection fraction decreased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Fibrin D dimer increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			
subjects affected / exposed	11 / 15 (73.33%)	11 / 15 (73.33%)	
occurrences (all)	15	25	
Platelet count decreased			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Protein total decreased			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	4	
Prothrombin time shortened			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	4 / 15 (26.67%)	4 / 15 (26.67%)	
occurrences (all)	6	4	
Weight increased			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
White blood cell count decreased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Urine output decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vitamin D decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Infusion related reaction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Cardiomyopathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cholinergic syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	3 / 15 (20.00%)	8 / 15 (53.33%)	
occurrences (all)	5	11	
Dysgeusia			
subjects affected / exposed	3 / 15 (20.00%)	3 / 15 (20.00%)	
occurrences (all)	3	3	
Headache			
subjects affected / exposed	2 / 15 (13.33%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Neuropathy peripheral			
subjects affected / exposed	2 / 15 (13.33%)	1 / 15 (6.67%)	
occurrences (all)	2	2	
Neurotoxicity			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 15 (26.67%)	4 / 15 (26.67%)	
occurrences (all)	5	6	
Polyneuropathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tension headache			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 15 (73.33%)	9 / 15 (60.00%)	
occurrences (all)	14	15	
Febrile neutropenia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Leukocytosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Leukopenia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	7	
Neutrophilia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	2	
Thrombocytopenia			
subjects affected / exposed	0 / 15 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Glaucoma			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 15 (33.33%)	5 / 15 (33.33%)	
occurrences (all)	6	9	
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	5	
Ascites			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Cheilitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Colitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	3 / 15 (20.00%)	
occurrences (all)	1	5	
Diarrhoea			
subjects affected / exposed	11 / 15 (73.33%)	14 / 15 (93.33%)	
occurrences (all)	16	25	
Dry mouth			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Dyspepsia			
subjects affected / exposed	5 / 15 (33.33%)	3 / 15 (20.00%)	
occurrences (all)	7	3	
Dysphagia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Enteritis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Eructation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastric ulcer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Ileus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	13 / 15 (86.67%)	11 / 15 (73.33%)	
occurrences (all)	18	20	
Oesophagitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pancreatitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	6 / 15 (40.00%)	9 / 15 (60.00%)	
occurrences (all)	8	15	
Tooth loss			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	3 / 15 (20.00%)	9 / 15 (60.00%)	
occurrences (all)	4	15	
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Decubitus ulcer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Nail ridging			
subjects affected / exposed	1 / 15 (6.67%)	3 / 15 (20.00%)	
occurrences (all)	1	3	
Onycholysis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Onychomadesis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	5 / 15 (33.33%)	5 / 15 (33.33%)	
occurrences (all)	6	7	
Pruritus			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Rash			

subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Skin hyperpigmentation			
subjects affected / exposed	3 / 15 (20.00%)	5 / 15 (33.33%)	
occurrences (all)	3	5	
Stasis dermatitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Azotaemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Haematuria			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Chronic kidney disease			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Endocrine disorders			
Hyperthyroidism			

subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Fracture pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)	3 / 15 (20.00%)	
occurrences (all)	1	3	
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	4 / 15 (26.67%)	
occurrences (all)	1	4	
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gingivitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hepatitis B			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Herpes simplex			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Herpes virus infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	3 / 15 (20.00%)	
occurrences (all)	1	3	
Oral herpes			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Tinea versicolour			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Toxocariasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	1	2	
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	9 / 15 (60.00%)	11 / 15 (73.33%)	
occurrences (all)	20	26	
Hyperglycaemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Hyperkalaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 15 (6.67%)	
occurrences (all)	1	3	
Hyperphosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	1 / 15 (6.67%)	4 / 15 (26.67%)	
occurrences (all)	1	5	
Hypocalcaemia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Hypochloraemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Hypokalaemia			
subjects affected / exposed	6 / 15 (40.00%)	3 / 15 (20.00%)	
occurrences (all)	6	3	
Hypomagnesaemia			
subjects affected / exposed	3 / 15 (20.00%)	8 / 15 (53.33%)	
occurrences (all)	4	10	
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	6	
Hypophosphataemia			
subjects affected / exposed	3 / 15 (20.00%)	2 / 15 (13.33%)	
occurrences (all)	3	7	
Hyposideraemia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	4	

Hypovitaminosis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0	1 / 15 (6.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2012	1. The "end of study" language was revised to ensure that the time needed for safety follow up assessments was incorporated 2. Clarified timing of pregnancy reporting within the Schedule of Assessments 3. Clarified the length of time for follow up of cardiac adverse events, symptomatic left ventricular ejection fraction (heart failure) and pregnancies after the last dose of study treatment, (corrected an inconsistency in the length of time for reporting AEs and SAEs after the last dose of study treatment from 6 months to 28 days) 4. Corrected the timeframe for administering a reloading dose of trastuzumab to 6 weeks, specified that the Study Management Team (SMT) would review the data according to the SMT Integrated Data Review Plan 5. Updated the SAE reporting time from within one business day to within 24 hours to align with the Sponsor's internal procedural document
24 May 2017	Because all patients have completed cardiac safety follow-up, a minor change was made to the protocol such that the study may end upon the Sponsor's decision to terminate the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported