Clinical trial results:
A Double-blind, Randomised, Parallel Group, Phase III Study to Demonstrate Equivalent Efficacy and Comparable Safety of CT-P6 and Herceptin, Both in Combination with Paclitaxel, in Patients with Metastatic Breast Cancer

Summary

EudraCT number	2009-016197-33
Trial protocol	AT PL BG
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	CT-P6 3.1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01084876
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celltrion, Inc.
Sponsor organisation address	23, Academy-ro, Yeonsu-gu, Incheon, Korea, Republic of, 22014
Public contact	Celltrion, Inc., Celltrion, Inc., 82 850 5000, contact@celltrion.com
Scientific contact	Celltrion, Inc., Celltrion, Inc., 82 850 5000, contact@celltrion.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	31 August 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 July 2012
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to demonstrate equivalence of CT-P6 and Herceptin, both given in combination with paclitaxel, in terms of efficacy determined by overall response rate (ORR).

Protection of trial subjects:

The study was conducted according to the protocol and in compliance with Good Clinical Practice (GCP) and other applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	40 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belarus: 16
Country: Number of subjects enrolled	Bulgaria: 20
Country: Number of subjects enrolled	Georgia: 21
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	India: 66
Country: Number of subjects enrolled	Korea, Republic of: 63
Country: Number of subjects enrolled	Latvia: 13
Country: Number of subjects enrolled	Malaysia: 5
Country: Number of subjects enrolled	Philippines: 32
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Romania: 13
Country: Number of subjects enrolled	Russian Federation: 86
Country: Number of subjects enrolled	Serbia: 9
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Thailand: 7
Country: Number of subjects enrolled	Turkey: 6
Country: Number of subjects enrolled	Ukraine: 107
Worldwide total number of subjects	475
EEA total number of subjects	54

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)	419
From 65 to 84 years	56
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled at 84 sites across Bulgaria, Poland, Romania, Ukraine, Russia, Georgia, Belarus, India, Turkey, Hong Kong, Singapore, Thailand, Malaysia, and the Philippines.

Pre-assignment

Screening details:

This study included females 18 years of age or older with Her-2 positive metastatic breast cancer who had not been treated in the first line metastatic setting.

Period 1

Period 1 title	Primary endpoint (8 cycle treatment) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	CT-P6

Arm description: -

Arm type	Experimental
Investigational medicinal product name	CT-P6
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Initial dose of 8 mg/kg, then at a dose of 6 mg/kg every three weeks

Arm title	Herceptin

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Herceptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Initial dose of 8 mg/kg, then at a dose of 6 mg/kg every three weeks

Number of subjects in period 1	CT-P6	Herceptin
Started	244	231
Completed	185	193
Not completed	59	38
Adverse event, serious fatal	2	2
Consent withdrawn by subject	4	-

Physician decision	2	-
Disease progression	41	21
Adverse event, non-fatal	8	6
Other	2	9

Baseline characteristics

Reporting groups	
Reporting group title	CT-P6
Reporting group description: -	
Reporting group title	Herceptin
Reporting group description: -	

Reporting group values	CT-P6	Herceptin	Total
Number of subjects	244	231	475
Age categorical Units: Subjects			
Adults (18-64 years)	210	209	419
From 65-84 years	34	22	56
85 years and over	0	0	0
Age continuous Units: years			
median	54.0	53.0	
full range (min-max)	31 to 75	25 to 78	-
Gender categorical Units: Subjects			
Female	244	231	475
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All randomised patients who received any study drug and had at least one post-baseline assessment, with the exception of the patients who violated against Herceptin indication

Reporting group values	Full Analysis Set (FAS)		
Number of subjects	475		
Age categorical Units: Subjects			
Adults (18-64 years)	419		
From 65-84 years	56		
85 years and over	0		
Age continuous Units: years			
median	54.0		
full range (min-max)	25 to 78		
Gender categorical Units: Subjects			
Female	475		
Male	0		

End points

End points reporting groups

Reporting group title	CT-P6
Reporting group description: -	
Reporting group title	Herceptin
Reporting group description: -	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All randomised patients who received any study drug and had at least one post-baseline assessment, with the exception of the patients who violated against Herceptin indication

Primary: Overall Response Rate at 6 Months

End point title	Overall Response Rate at 6 Months

End point description:

End point type	Primary

End point timeframe:

6 months

End point values	CT-P6	Herceptin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244[1]	231[2]		
Units: Number of patients with CR or PR				
ORR (CR or PR)	138	143		

Notes:

[1] - Full Analysis Set (FAS)

[2] - Full Analysis Set (FAS)

Statistical analyses

Statistical analysis title	ORR at 6 month
Comparison groups	Herceptin v CT-P6
Number of subjects included in analysis	475
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Parameter estimate	Risk difference (RD)
Point estimate	-0.0535
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.143
upper limit	0.036

Notes:

[3] - Equivalence margin (-0.15, 0.15)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2 years

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13

Reporting groups

Reporting group title	CT-P6
Reporting group description: -	
Reporting group title	Herceptin

Reporting group description: -

Serious adverse events	CT-P6	Herceptin	
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 244 (13.93%)	37 / 231 (16.02%)	
number of deaths (all causes)	117	121	
number of deaths resulting from adverse events	8	8	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant pleural effusion			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 244 (0.00%)	3 / 231 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Biliary drainage			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract operation			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extended radical mastectomy			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastectomy			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (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			
Death			
subjects affected / exposed	0 / 244 (0.00%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Disease progression			
subjects affected / exposed	4 / 244 (1.64%)	6 / 231 (2.60%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 4	0 / 3	
Inflammation			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infusion related reaction			
subjects affected / exposed	2 / 244 (0.82%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 244 (0.82%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 244 (0.82%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval ulceration			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
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			
Dyspnoea			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure acute			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	

Cardiac failure congestive			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	2 / 244 (0.82%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 244 (0.41%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	5 / 244 (2.05%)	4 / 231 (1.73%)	
occurrences causally related to treatment / all	2 / 5	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 244 (0.82%)	6 / 231 (2.60%)	
occurrences causally related to treatment / all	0 / 2	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	

Thrombocytopenia			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 244 (0.41%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Leukocytoclastic vasculitis			

subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	2 / 244 (0.82%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 244 (0.41%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutropenic infection			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 244 (0.82%)	3 / 231 (1.30%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 244 (0.41%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 244 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CT-P6	Herceptin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 244 (92.62%)	214 / 231 (92.64%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	23 / 244 (9.43%)	24 / 231 (10.39%)	
occurrences (all)	51	50	
Aspartate aminotransferase increased			
subjects affected / exposed	17 / 244 (6.97%)	15 / 231 (6.49%)	
occurrences (all)	28	24	
Blood alkaline phosphatase increased			

subjects affected / exposed	13 / 244 (5.33%)	10 / 231 (4.33%)	
occurrences (all)	18	18	
Gamma-glutamyltransferase increased			
subjects affected / exposed	18 / 244 (7.38%)	12 / 231 (5.19%)	
occurrences (all)	39	27	
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 244 (4.10%)	14 / 231 (6.06%)	
occurrences (all)	12	19	
Nervous system disorders			
Dizziness			
subjects affected / exposed	17 / 244 (6.97%)	24 / 231 (10.39%)	
occurrences (all)	24	35	
Headache			
subjects affected / exposed	21 / 244 (8.61%)	33 / 231 (14.29%)	
occurrences (all)	26	46	
Neuropathy peripheral			
subjects affected / exposed	65 / 244 (26.64%)	57 / 231 (24.68%)	
occurrences (all)	147	130	
Paraesthesia			
subjects affected / exposed	15 / 244 (6.15%)	9 / 231 (3.90%)	
occurrences (all)	16	18	
Peripheral sensory neuropathy			
subjects affected / exposed	50 / 244 (20.49%)	54 / 231 (23.38%)	
occurrences (all)	125	85	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	31 / 244 (12.70%)	38 / 231 (16.45%)	
occurrences (all)	58	67	
Leukopenia			
subjects affected / exposed	28 / 244 (11.48%)	50 / 231 (21.65%)	
occurrences (all)	40	85	
Neutropenia			
subjects affected / exposed	68 / 244 (27.87%)	76 / 231 (32.90%)	
occurrences (all)	126	152	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	49 / 244 (20.08%)	34 / 231 (14.72%)	
occurrences (all)	108	52	
Chills			
subjects affected / exposed	10 / 244 (4.10%)	19 / 231 (8.23%)	
occurrences (all)	15	20	
Fatigue			
subjects affected / exposed	30 / 244 (12.30%)	34 / 231 (14.72%)	
occurrences (all)	78	62	
Oedema peripheral			
subjects affected / exposed	10 / 244 (4.10%)	13 / 231 (5.63%)	
occurrences (all)	13	18	
Pain			
subjects affected / exposed	11 / 244 (4.51%)	16 / 231 (6.93%)	
occurrences (all)	17	31	
Pyrexia			
subjects affected / exposed	23 / 244 (9.43%)	28 / 231 (12.12%)	
occurrences (all)	40	42	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	14 / 244 (5.74%)	13 / 231 (5.63%)	
occurrences (all)	20	14	
Constipation			
subjects affected / exposed	10 / 244 (4.10%)	18 / 231 (7.79%)	
occurrences (all)	14	22	
Diarrhoea			
subjects affected / exposed	34 / 244 (13.93%)	44 / 231 (19.05%)	
occurrences (all)	52	74	
Nausea			
subjects affected / exposed	41 / 244 (16.80%)	40 / 231 (17.32%)	
occurrences (all)	129	74	
Stomatitis			
subjects affected / exposed	14 / 244 (5.74%)	16 / 231 (6.93%)	
occurrences (all)	25	19	
Vomiting			

subjects affected / exposed	23 / 244 (9.43%)	27 / 231 (11.69%)	
occurrences (all)	34	37	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	25 / 244 (10.25%)	22 / 231 (9.52%)	
occurrences (all)	34	31	
Dyspnoea			
subjects affected / exposed	13 / 244 (5.33%)	10 / 231 (4.33%)	
occurrences (all)	19	13	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	122 / 244 (50.00%)	127 / 231 (54.98%)	
occurrences (all)	153	151	
Pruritus			
subjects affected / exposed	10 / 244 (4.10%)	18 / 231 (7.79%)	
occurrences (all)	14	24	
Rash			
subjects affected / exposed	19 / 244 (7.79%)	15 / 231 (6.49%)	
occurrences (all)	27	38	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	11 / 244 (4.51%)	16 / 231 (6.93%)	
occurrences (all)	18	19	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	22 / 244 (9.02%)	33 / 231 (14.29%)	
occurrences (all)	82	123	
Back pain			
subjects affected / exposed	15 / 244 (6.15%)	20 / 231 (8.66%)	
occurrences (all)	20	30	
Bone pain			
subjects affected / exposed	24 / 244 (9.84%)	17 / 231 (7.36%)	
occurrences (all)	63	30	
Musculoskeletal pain			
subjects affected / exposed	9 / 244 (3.69%)	13 / 231 (5.63%)	
occurrences (all)	10	21	

Myalgia			
subjects affected / exposed	47 / 244 (19.26%)	53 / 231 (22.94%)	
occurrences (all)	173	167	
Pain in extremity			
subjects affected / exposed	23 / 244 (9.43%)	31 / 231 (13.42%)	
occurrences (all)	36	49	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	8 / 244 (3.28%)	13 / 231 (5.63%)	
occurrences (all)	11	17	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	19 / 244 (7.79%)	16 / 231 (6.93%)	
occurrences (all)	37	30	
Hypercholesterolaemia			
subjects affected / exposed	8 / 244 (3.28%)	14 / 231 (6.06%)	
occurrences (all)	23	24	
Hyperglycaemia			
subjects affected / exposed	10 / 244 (4.10%)	15 / 231 (6.49%)	
occurrences (all)	31	36	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2010	Amendments in the eligibility crieria and procedures
03 July 2013	The blinded study drug information was opened

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.

The study is planned to analyze the data from both phase I/IIa and III and data collected from phase III are not analyzed separately.

Notes: