Clinical trial results:
Phase 2 Study of Pemetrexed and Cisplatin as Induction, Followed by Pemetrexed and Cisplatin with Concurrent Thoracic Radiotherapy, in Patients with Unresectable Locally-Advanced Stage III, Non-Squamous, Non-Small Cell Lung Cancer

Summary

EudraCT number	2009-011739-11
Trial protocol	FR ES IT DE
Global end of trial date	23 July 2013

Results information

Result version number	v1 (current)
This version publication date	04 July 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	H3E-EW-S128

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01000480
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Alias: H3E-EW-S128, Trial ID: 13099

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Cemter, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 Am - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 Am - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	23 July 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study is to assess the antitumor activity as measured by progression free survival 1 year after start of treatment with study drug.

Protection of trial subjects:

This study was conducted in accordance with International Code of Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy:

Concurrent radiation therapy and chemotherapy is the accepted standard of care for most patients with locally advanced, unresectable Stage III Non-Small Cell Lung Cancer.

Evidence for comparator: -

Actual start date of recruitment	29 October 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Italy: 22
Worldwide total number of subjects	90
EEA total number of subjects	90

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	59
From 65 to 84 years	31
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study treatment had 2 phases and follow-up. Induction phase: 2 cycles of pemetrexed-cisplatin. Then, if eligible, the concurrent phase: 2 more cycles of pemetrexed-cisplatin and thoracic radiotherapy. Follow-up period: Started when treatment discontinued or completed, and lasted up to 2 years after first dose of pemetrexed.

Period 1

Period 1 title	Induction Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Induction phase

Arm description:

Pemetrexed: 500 milligrams per square meter (mg/m²) intravenous infusion on Day 1 of 21-day cycle.
Cisplatin: 75 mg/m² intravenous infusion on Day 1 of 21-day cycle.

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	LY231514, Alimta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Drug: Pemetrexed
500 milligrams per square meter (mg/m²) intravenous infusion on Day 1 of a 21 day cycle for 2 cycles: with possibility of 2 additional cycles.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Drug: Cisplatin
75 mg/m² intravenous infusion on Day 1 of a 21 day cycle for 2 cycles; with the possibility of 2 additional cycles.

Number of subjects in period 1	Induction phase
Started	90
Received at Least 1 Dose of Either Drug	90
Entered Follow-Up Period	88
Completed	83
Not completed	7

Physician decision	1
Adverse event, non-fatal	2
Lost to follow-up	1
Entry Criteria Not Met	3

Period 2

Period 2 title	Concurrent Therapy Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Concurrent Therapy Phase

Arm description:

Participants eligible for concurrent phase (2 more cycles of pemetrexed-cisplatin treatment and radiotherapy) if they had complete response, partial response, or stable disease (Response Evaluation Criteria in Solid Tumors guidelines), total lung volume receiving more than 20 gray (Gy) ≤35% (dose volume histogram), 0 or 1 Eastern Cooperative Oncology Group performance status, no residual neurological toxicity >Grade 2 (Common Terminology Criteria for Adverse Events).

Thoracic Radiotherapy: 2 Gy/fraction after completion of pemetrexed and cisplatin infusions on Day 1 of Cycle 3 and continued daily (5 days per week) until total delivered dose was 66 Gy, over approximately 7 weeks.

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	LY231514, Alimta
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed: 500 milligrams per square meter (mg/m²) intravenous infusion on Day 1 of 21-day cycle.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin: 75 mg/m² intravenous infusion on Day 1 of 21-day cycle.

Number of subjects in period 2[1]	Concurrent Therapy Phase
Started	75
Completed	65
Not completed	10
Physician decision	1
Adverse event, non-fatal	4
Withdrawal by Subject	3
Protocol Violation	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants who died (any cause) or had disease progression are considered to have completed phase. Eight participants who completed the Induction Phase were not eligible for the Concurrent Therapy Phase.

Baseline characteristics

Reporting groups	
Reporting group title	Induction Phase
Reporting group description:	
Pemetrexed: 500 milligrams per square meter (mg/m²) intravenous infusion on Day 1 of 21-day cycle. Cisplatin: 75 mg/m² intravenous infusion on Day 1 of 21-day cycle.	

Reporting group values	Induction Phase	Total	
Number of subjects	90	90	
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)	59	59	
From 65-84 years	31	31	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	61.7		
standard deviation	± 8.15	-	
Gender categorical Units: Subjects			
Female	39	39	
Male	51	51	
Race/Ethnicity Units: Subjects			
White	90	90	
Region of Enrollment Units: Subjects			
France	9	9	
Spain	17	17	
Germany	42	42	
Italy	22	22	
Stage of Disease			
[1] Classification based on American Joint Committee on Cancer (AJCC) Staging System for lung cancer (sixth edition, 2002). Disease stage means how big the tumor is and how far it has spread. Stages range from 0 (not spread) to IV (spread throughout the body). Stage IIIA is a locally advanced cancer that spread to lymph nodes within the chest area. Stage IIIB is a locally advanced cancer that spread to nearby tissue or far away lymph nodes, or has fluid, containing cancer cells, built up between the layers lining the lungs.			
Units: Subjects			
Stage IIIA	32	32	
Stage IIIB	56	56	
Stage IV	2	2	

Eastern Cooperative Oncology Group (ECOG) performance status (PS)			
[2] ECOG PS classified participants according to their functional impairment. Scores ranged from 0 (Fully Active) to 5 (Death). 0=Fully Active; 1=Ambulatory, Restricted Strenuous Activity; 2=Ambulatory, No Work Activities; 3=Partially Confined to Bed, Limited Self Care; 4=Completely Disabled; and 5=Death.			
Units: Subjects			
ECOG PS=0	59	59	
ECOG PS=1	31	31	
ECOG PS=2	0	0	
Initial Pathological Diagnosis			
[3] The number of participants with an initial pathological diagnosis of Adenocarcinoma (lung), Carcinoma (large cell, lung), Carcinoma [non-small cell, lung, not otherwise specified (NOS)], Carcinoma (non-small cell, lung, poorly differentiated).			
Units: Subjects			
Adenocarcinoma (lung)	81	81	
Carcinoma (large cell, lung)	7	7	
Carcinoma (non-small cell, lung, NOS)	1	1	
Carcinoma (non-small cell, poorly differentiated)	1	1	
Current Tobacco Use Units: Subjects			
Never used tobacco	7	7	
Former user of tobacco	55	55	
Current use of tobacco	28	28	

End points

End points reporting groups

Reporting group title	Induction phase

Reporting group description:

Pemetrexed: 500 milligrams per square meter (mg/m²) intravenous infusion on Day 1 of 21-day cycle.
Cisplatin: 75 mg/m² intravenous infusion on Day 1 of 21-day cycle.

Reporting group title	Concurrent Therapy Phase

Reporting group description:

Participants eligible for concurrent phase (2 more cycles of pemetrexed-cisplatin treatment and radiotherapy) if they had complete response, partial response, or stable disease (Response Evaluation Criteria in Solid Tumors guidelines), total lung volume receiving more than 20 gray (Gy) ≤35% (dose volume histogram), 0 or 1 Eastern Cooperative Oncology Group performance status, no residual neurological toxicity >Grade 2 (Common Terminology Criteria for Adverse Events).

Thoracic Radiotherapy: 2 Gy/fraction after completion of pemetrexed and cisplatin infusions on Day 1 of Cycle 3 and continued daily (5 days per week) until total delivered dose was 66 Gy, over approximately 7 weeks.

Primary: 1 Year Progression Free Survival (PFS)

End point title	1 Year Progression Free Survival (PFS)[1]

End point description:

Unable to provide statistical analysis of comparison groups for a single group assignment study due to system limitations.

End point type	Primary

End point timeframe:

Date of first dose to date of objectively determined PD or death [every cycle up to 4 cycles and then every 3 months up to 1 year (1 cycle=21 days)]

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: System prevents Statistical Analyses (SA) comparing investigational regimen to historical data.
SA for 1 Year PFS. Reporting Group 1: Induction phase
Analysis description: Null hypothesis (H0): 1-year PFS ≤45% and the alternative hypothesis (H1): 1-year PFS ≥60%, at a 2-sided alpha level of 5%, assuming that PFS time followed an exponential distribution.
P-value = 0.0645
P-value for H0 which compared the investigational regimen to historical data.
Method: Maximum likelihood estimate

End point values	Induction phase			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: Percent of Participants				
number (confidence interval 95%)	53.7 (44.8 to 62.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival (OS) was the duration from enrollment to death due to any cause. Participants who were alive were censored at the last contact.
[1] The upper 95% confidence interval was not calculable because an insufficient number of participants reached the event at the final time point for assessment.

End point type	Secondary

End point timeframe:

Date of first dose to date of death (up to 35.4 months)

End point values	Induction phase			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: Participants				
median (confidence interval 95%)	26.2 (16.7 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With an Objective Tumor Response

End point title	Number of Participants With an Objective Tumor Response

End point description:

Participants with confirmed complete response (CR), confirmed partial response (PR), stable disease (SD), or progressive disease (PD) according to Response Evaluation Criteria In Solid Tumors (RECIST, version 1.0) criteria, as well as participants with a not evaluable/tumor response unknown. CR: disappearance of all tumor lesions. PR: either a) at least a 30% decrease in sum of longest diameter (LD) of target lesions taking as a reference baseline sum LDs, or b) complete disappearance of target lesions, with persistence (not worsening) of 1 or more nontarget lesions. In either case, no new lesions appeared. SD: small changes that did not meet above criteria. PD: at least a 20% increase in sum of LD of target lesions taking as reference smallest sum LD recorded since treatment started or appearance of 1 or more new lesions.
Participants who discontinued study treatment (for reasons other than progression) before entering concurrent phase were considered to have non-evaluable response

End point type	Secondary

End point timeframe:

Date of first dose through end of follow-up [up to 30 weeks (1 cycle=21 days)]

End point values	Induction phase			
Subject group type	Reporting group			
Number of subjects analysed	90			
Units: Participants				
number (not applicable)				
Complete Response	9			
Partial Response	45			
Stable Disease	16			
Disease Progression	12			
Not evaluable/Response unknown	8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

H3E-EW-S128

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Pemetrexed 500 mg/m2 + Cisplatin 75 mg/m2 + Radiotherapy 66 g

Reporting group description: -

Serious adverse events	Pemetrexed 500 mg/m2 + Cisplatin 75 mg/m2 + Radiotherapy 66 g		
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 90 (25.56%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
radiation oesophagitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	8 / 90 (8.89%)		
occurrences causally related to treatment / all	2 / 9		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
paraesthesia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
syncope				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
asthenia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
general physical health deterioration				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 90 (2.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
pyrexia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
leukopenia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
hypoacusis				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
enteritis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
gastritis erosive			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
nausea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
pulmonary embolism			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 90 (4.44%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
renal impairment			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
urinary retention				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
device related infection				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pneumonia				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
septic shock				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 90 (1.11%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Metabolism and nutrition disorders				
dehydration				
alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 90 (2.22%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
hyponatraemia				
alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 90 (1.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pemetrexed 500 mg/m2 + Cisplatin 75 mg/m2 + Radiotherapy 66 g		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 90 (87.78%)		
Investigations			
haemoglobin decreased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	7 / 90 (7.78%)		
occurrences (all)	7		
neutrophil count decreased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 90 (5.56%)		
occurrences (all)	6		
white blood cell count decreased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 90 (5.56%)		
occurrences (all)	7		
Injury, poisoning and procedural complications			
radiation oesophagitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	10 / 90 (11.11%)		
occurrences (all)	10		
radiation skin injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	10 / 90 (11.11%)		
occurrences (all)	10		
Nervous system disorders			

dizziness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	7 / 90 (7.78%)		
occurrences (all)	7		
dysgeusia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	7 / 90 (7.78%)		
occurrences (all)	9		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	7 / 90 (7.78%)		
occurrences (all)	8		
leukopenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	12 / 90 (13.33%)		
occurrences (all)	13		
lymphopenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	6 / 90 (6.67%)		
occurrences (all)	11		
neutropenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	17 / 90 (18.89%)		
occurrences (all)	22		
thrombocytopenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 90 (5.56%)		
occurrences (all)	5		
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	18 / 90 (20.00%)		
occurrences (all)	23		
chest pain			

alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 90 (5.56%)		
occurrences (all)	8		
fatigue			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	14 / 90 (15.56%)		
occurrences (all)	16		
pyrexia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	8 / 90 (8.89%)		
occurrences (all)	10		
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	6 / 90 (6.67%)		
occurrences (all)	6		
Eye disorders			
conjunctivitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	6 / 90 (6.67%)		
occurrences (all)	6		
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	22 / 90 (24.44%)		
occurrences (all)	26		
diarrhoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	8 / 90 (8.89%)		
occurrences (all)	8		
dyspepsia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	7 / 90 (7.78%)		
occurrences (all)	7		
dysphagia			

alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	27 / 90 (30.00%)		
occurrences (all)	27		
nausea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	43 / 90 (47.78%)		
occurrences (all)	67		
oesophagitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	23 / 90 (25.56%)		
occurrences (all)	25		
stomatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	10 / 90 (11.11%)		
occurrences (all)	12		
vomiting			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	11 / 90 (12.22%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	14 / 90 (15.56%)		
occurrences (all)	14		
dyspnoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	13 / 90 (14.44%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
rash			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	6 / 90 (6.67%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			

back pain alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	 6 / 90 (6.67%) 6		
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	 8 / 90 (8.89%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported