Clinical trial results:
A multicenter, randomized, double-blind, placebo-controlled phase III trial of tecemotide versus placebo in subjects with completed concurrent chemo-radiotherapy for unresectable stage III non-small cell lung cancer (NSCLC)

Summary

EudraCT number	2013-003760-30
Trial protocol	CZ AT BE DE SE PT IT IE SK ES PL
Global end of trial date	02 July 2015

Results information

Result version number	v1 (current)
This version publication date	10 July 2016
First version publication date	10 July 2016

Trial information

Trial identification

Sponsor protocol code	EMR 63325-021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02049151
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck KGaA
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Merck KGaA Communication Centre, Merck KGaA, +49 6151725200, service@merckgroup.com
Scientific contact	Merck KGaA Communication Centre, Merck KGaA, +49 6151725200, service@merckgroup.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	02 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2015
Global end of trial reached?	Yes
Global end of trial date	02 July 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This is a multi-center, double-blind, placebo-controlled, randomized, Phase 3 trial in subjects with unresectable stage III non-small cell lung cancer (NSCLC) who have demonstrated either stable disease or objective response following primary concurrent chemo-radiotherapy (CRT), comparing overall survival (OS) time in subjects treated with tecemotide versus subjects treated with tecemotide-matching placebo.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	35
EEA total number of subjects	7

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)	17
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First/last subject(informed consent): 21 Mar 2014/11 Sep 2014. Study completion date: 02 Jul 2015.

Pre-assignment

Screening details:

50 subjects were screened for eligibility; 15 excluded (mainly due to non-fulfillment of inclusion or exclusion criteria) and 35 subjects were randomized. Three subjects were randomized but were not treated.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Tecemotide (L-BLP25) + Cyclophosphamide

Arm description:

Single dose of cyclophosphamide was administered intravenously, 3 days prior to the tecemotide dosing, tecemotide (L-BLP25) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with tecemotide (L-BLP25) (806 mcg) were administered every 6 weeks until disease progression was documented.

Arm type	Experimental
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received single dose of cyclophosphamide (300 milligrams per square meter [mg/m^2] to a maximum of 600mg)

Investigational medicinal product name	Tecemotide (L-BLP25)
Investigational medicinal product code	EMD531444
Other name	BLP25 lipopeptide
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received subcutaneous vaccinations with 806 mcg of tecemotide (L-BLP25) .

Arm title	Placebo + Saline

Arm description:

Single dose of saline was administered intravenously, 3 days prior to the tecemotide dosing, placebo doses matched to tecemotide (L-BLP25) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with placebo were administered every 6 weeks until disease progression was documented.

Arm type	Active comparator

Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received single dose of saline (sodium chloride, 9 gram per liter (g/L) was administered intravenously.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received placebo doses matched to tecemotide (L-BLP25) was administered subcutaneously.

Number of subjects in period 1[1]	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline
Started	15	17
Completed	15	17

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Three subjects were randomized but were not treated. 2 subjects from Tecemotide (L-BLP25) + Cyclophosphamide arm and 1 subjects from Placebo + Saline arm.

Baseline characteristics

Reporting groups	
Reporting group title	Tecemotide (L-BLP25) + Cyclophosphamide

Reporting group description:

Single dose of cyclophosphamide was administered intravenously, 3 days prior to the tecemotide dosing, tecemotide (L-BLP25) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with tecemotide (L-BLP25) (806 mcg) were administered every 6 weeks until disease progression was documented.

Reporting group title	Placebo + Saline

Reporting group description:

Single dose of saline was administered intravenously, 3 days prior to the tecemotide dosing, placebo doses matched to tecemotide (L-BLP25) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with placebo were administered every 6 weeks until disease progression was documented.

Reporting group values	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline	Total
Number of subjects	15	17	32
Age Categorical Units: Subjects			
Greater than equal to (<=) 18 Years	0	0	0
Between 18 and 65 Years	5	10	15
Less than equal to (>=) 65 Years	10	7	17
Age Continuous Units: years			
arithmetic mean	66.2	63.9	
standard deviation	± 5.99	± 10.45	-
Gender, Male/Female Units: Subjects			
Female	2	7	9
Male	13	10	23

End points

End points reporting groups

Reporting group title	Tecemotide (L-BLP25) + Cyclophosphamide

Reporting group description:

Single dose of cyclophosphamide was administered intravenously, 3 days prior to the tecemotide dosing, tecemotide (L-BLP25) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with tecemotide (L-BLP25) (806 mcg) were administered every 6 weeks until disease progression was documented.

Reporting group title	Placebo + Saline

Reporting group description:

Single dose of saline was administered intravenously, 3 days prior to the tecemotide dosing, placebo doses matched to tecemotide (L-BLP25) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with placebo were administered every 6 weeks until disease progression was documented.

Primary: Overall Survival Time

End point title	Overall Survival Time[1]

End point description:

Overall Survival time was defined as the time from randomization to death. Subjects without event were censored at the last date known to be alive or date lost to follow-up, whichever was earlier. Due to termination of the study as a consequence of the discontinuation of the clinical development of tecemotide, the outcome measure was not analyzed.

End point type	Primary

End point timeframe:

Time from date of randomization until death, assessed maximum up to 16 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistics were performed for this endpoint, only descriptive statistics was reported for this endpoint.

End point values	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: months				
median (full range (min-max))	(to)	(to)		

Notes:

[2] - Due to termination of the study the outcome measure was not analyzed.

[3] - Due to termination of the study the outcome measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Symptom Progression (TTSP)

End point title	Time to Symptom Progression (TTSP)

End point description:

TTSP was measured using the Lung Cancer Symptom Scale (LCSS). Symptomatic progression was defined as an increase (worsening) of the Average Symptomatic Burden Index (ASBI, the mean of the

six major lung cancer specific symptom scores of the LCSS scale – ranging from 0 to 100, where higher score indicates worst outcome). Worsening was defined as a 10% increase in the scale breadth from the baseline score. TTSP was defined as the time from randomization to worsening in ASBI. Subjects without event were censored at the date of the last LCSS assessment.Due to termination of the study as a consequence of the discontinuation of the clinical development of tecemotide, outcome measure was not analysed.

End point type	Secondary

End point timeframe:

Time from date of randomization until progressive disease (PD), assessed up to 16 months

End point values	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: months				
median (full range (min-max))	(to)	(to)		

Notes:

[4] - Due to termination of the study the outcome measure was not analyzed.

[5] - Due to termination of the study the outcome measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the time from date of randomization until date of the first documentation of PD or death due to any cause in the absence of documented PD, whichever occurred first. PFS was assessed as per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1). PD was defined as at least a 20% increase in the sum of longest diameter (SLD), taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. Subjects without event were censored on the date of last tumor assessment. Due to termination of the study as a consequence of the discontinuation of the clinical development of tecemotide, the outcome measure was not analyzed.

End point type	Secondary

End point timeframe:

Time from date of randomization until PD or death, assessed up to 16 months

End point values	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: months				
median (full range (min-max))	(to)	(to)		

Notes:

[6] - Due to termination of the study the outcome measure was not analyzed.

[7] - Due to termination of the study the outcome measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)

End point description:

TTP was measured from the date of randomization to the date of tumor progression. Date of tumor progression was date of radiological diagnosis of PD, performed as per RECIST 1.1. PD is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of 1 or more new lesions is also considered progression. For participants alive without tumor progression at time of analysis, the time between date of randomization and date of last trial treatment was calculated and used as a censored observation in the analysis. Subjects dying from causes other than PD was censored at time of death. Due to termination of the study as a consequence of the discontinuation of the clinical development of tecemotide, outcome measure was not analysed.

End point type	Secondary

End point timeframe:

Time from date of randomization until PD, assessed up to 16 months

End point values	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: months				
median (full range (min-max))	(to)	(to)		

Notes:

[8] - Due to termination of the study the outcome measure was not analyzed.

[9] - Due to termination of the study the outcome measure was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, National Cancer Institute-Common Toxicity Criteria (NCI−CTC)Grade 3/4 TEAEs, TEAEs Leading to Permanent Discontinuation, TEAEs Leading to Death, Injection Site Reactions (ISRs)

End point title	Number Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, National Cancer Institute-Common Toxicity Criteria (NCI−CTC)Grade 3/4 TEAEs, TEAEs Leading to Permanent Discontinuation, TEAEs Leading to Death, Injection Site Reactions (ISRs)

End point description:

An adverse event (AE) was defined as any new untoward medical occurrences/worsening of pre-existing medical condition, whether or not related to study drug. A serious TEAE was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect. TEAEs occurred between the first dose of study drug and up to 42 days after the last dose that were absent before treatment or that worsened relative to pretreatment state. Number of Subjects With TEAEs, Serious TEAEs, NCI−CTC Grade 3/4 TEAEs, TEAEs Leading to Permanent Discontinuation, TEAEs Leading to Death, and ISRs were reported. Safety Analysis Set included all subjects who had taken at least one dose of trial treatment (tecemotide [L-BLP25] or placebo), including cyclophosphamide or saline.

End point type	Secondary

End point timeframe:

Time from first dose up to 42 days after the last dose of the trial treatment: assessed maximum up to 16 months

End point values	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	17		
Units: subjects				
number (not applicable)				
TEAEs	14	13		
Serious TEAEs	4	1		
Grade 3 or 4 TEAEs	5	2		
TEAEs Leading to Permanent Discontinuation	2	1		
TEAEs leading to death	0	0		
ISRs	0	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Time from first dose up to 42 days after the last dose of the trial treatment: assessed maximum up to 16 months.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Tecemotide (L-BLP25) + Cyclophosphamide

Reporting group description:

Single dose of cyclophosphamide (300 milligrams per square meter [mg/m^2] to a maximum of 600 mg) was administered intravenously, 3 days prior to the tecemotide dosing, tecemotide (L-BLP25) (806 micrograms [mcg]) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with tecemotide (L-BLP25) (806 mcg) were administered every 6 weeks until disease progression was documented

Reporting group title	Placebo + Saline

Reporting group description:

Single dose of saline (sodium chloride, 9 grams per liter [g/L]) was administered intravenously, 3 days prior to the tecemotide dosing, placebo doses matched to tecemotide (L-BLP25) was administered weekly subcutaneously for 8 weeks, followed by a maintenance treatment phase starting at Week 14, in which subcutaneous vaccinations with placebo were administered every 6 weeks until disease progression was documented.

Serious adverse events	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 15 (26.67%)	1 / 17 (5.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 15 (20.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Tecemotide (L-BLP25) + Cyclophosphamide	Placebo + Saline	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)	13 / 17 (76.47%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	3 / 15 (20.00%)	3 / 17 (17.65%)	
occurrences (all)	3	3	
Feeling hot			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			

subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Injection site bruising			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Injection site hypoaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Pain			
subjects affected / exposed	0 / 15 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	2 / 15 (13.33%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Dyspnoea exertional			
subjects affected / exposed	2 / 15 (13.33%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Hypoxia			

subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Laryngeal inflammation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	2 / 15 (13.33%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Nasal congestion			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Productive cough			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	2 / 17 (11.76%)	
occurrences (all)	0	2	
Rhinitis allergic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Mood altered			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Weight decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
White blood cell count decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 15 (6.67%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Contusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Radiation pneumonitis			
subjects affected / exposed	2 / 15 (13.33%)	0 / 17 (0.00%)	
occurrences (all)	2	0	
Periorbital haematoma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Hypoaesthesia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Hyperaesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Psychomotor hyperactivity			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Tension headache			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Leukocytosis			

subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Food poisoning			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	2 / 15 (13.33%)	2 / 17 (11.76%)	
occurrences (all)	2	2	
Faecal incontinence			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Gingival pain			

subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Palmar erythema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Pain of skin			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 15 (13.33%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Groin pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	2 / 15 (13.33%)	1 / 17 (5.88%)	
occurrences (all)	2	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Myalgia			

subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	1 / 17 (5.88%)	
occurrences (all)	1	1	
Pharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 17 (5.88%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 15 (6.67%)	2 / 17 (11.76%)	
occurrences (all)	1	2	
Hypomagnesaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	
Dehydration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 17 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2014	-The EORTC QLQ C30 was added at the same time points as other QoL questionnaires. The additional questionnaire will further support evaluation of QoL especially considering assessment of general health status aspects. -Subjects with a known history of hepatitis are to be excluded from the trial. To implement a pro-active testing approach and to avoid the risk of exposing subjects potentially suffering from infectious hepatitis and for whom no specific hepatitis B virus (HBV) and/or hepatitis C virus (HCV) diagnostic procedures were recently conducted by clinical sites before trial screening, the corresponding virology blood tests were added. A mandatory HBV and a mandatory HCV test to be performed by a central laboratory will be implemented at screening and, taking into account the disease biology, at Week 32. -Subjects with acquired immunodeficiencies are to be excluded from the trial. To implement a pro-active testing approach and to avoid exposing subjects potentially suffering from HIV infection and for whom no specific HIV diagnostic procedures were recently conducted by clinical sites before trial screening, the corresponding virology blood test was added. A mandatory HIV test to be performed by a central laboratory will be implemented at screening and, taking into account the disease biology, at Week 14. - The rationale for the dosing regimen used in the current study was not specifically noted. A rationale for the dosing was added to Section 3.2 of the clinical trial protocol. -The birth control wording in the clinical trial protocol specified that subjects of childbearing potential would be required to use an adequate form of birth control but did not clearly define adequate contraception. The standard definition for highly effective methods of birth control was added.

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.

Sponsor discontinued development of tecemotide (L-BLP25) in NSCLC, hence the study was terminated.

Notes: