Clinical trial results:
A PHASE II, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY EVALUATING THE SAFETY AND EFFICACY OF MEGF0444A IN COMBINATION WITH CARBOPLATIN, PACLITAXEL AND BEVACIZUMAB IN PATIENTS WITH ADVANCED OR RECURRENT NON-SQUAMOUS NON-SMALL CELL LUNG CANCER WHO HAVE NOT RECEIVED PRIOR CHEMOTHERAPY FOR ADVANCED DISEASE

Summary

EudraCT number	2011-000711-85
Trial protocol	CZ HU
Global end of trial date	29 August 2013

Results information

Result version number	v1 (current)
This version publication date	02 July 2016
First version publication date	02 July 2016

Trial information

Trial identification

Sponsor protocol code	GO27811

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01366131
WHO universal trial number (UTN)	-
Other trial identifiers	Genentech Study ID: MEF4984g

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124,, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, 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	12 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 August 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This is a Phase II, multicenter, randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy, safety, and pharmacokinetics (PK) of MEGF0444A combined with paclitaxel + carboplatin + bevacizumab therapy in participants with histologically or cytologically documented inoperable, locally advanced, metastatic (Stage IV), or recurrent non-squamous non-small cell lung cancer (NSCLC). The primary objective of this trial was to evaluate the efficacy of MEGF0444A in combination with carboplatin, paclitaxel, and bevacizumab in participants with advanced or recurrent non-squamous NSCLC, as measured by progression free survival (PFS).

Protection of trial subjects:

This study was conducted in accordance with the United States Food and Drug Administration (USFDA) regulations, the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP), and applicable local, state, and federal laws, as well as other applicable country laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	United States: 33
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Czech Republic: 2
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Hungary: 20
Worldwide total number of subjects	104
EEA total number of subjects	68

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)	57
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

104 participants who met the study selection criteria were enrolled and randomized to one of the two treatment arms, MEGF0444A and Placebo. Control arm (52 participants): Placebo + Paclitaxel + Carboplatin + Bevacizumab; Experimental arm (52 participants): MEGF044A + Paclitaxel + Carboplatin Bevacizumab.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MEGF0444A

Arm description:

Participants received paclitaxel 200 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1, carboplatin (at doses to achieve an area under the concentration time curve [AUC] of 6 milligrams/milliliter*minute [mg/mL*min]) IV infusion on Day 1, and bevacizumab 15 milligrams per kilogram (mg/kg) IV infusion on Day 1 of each 21-day cycle. Participants also received MEGF0444A at a fixed dose of 600 mg IV infusion on Day 1 of Cycle 1, followed by subsequent doses of 600 mg every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by MEGF0444A. Paclitaxel and carboplatin were administered until disease progression (DP) or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and MEGF0444A were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

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

Dosage and administration details:

Participants received paclitaxel 200 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or unacceptable toxicity, for a maximum of 6 cycles.

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

Dosage and administration details:

Participants received carboplatin (at doses to achieve an AUC of 6 mg/mL*min) IV infusion on Day 1 of each 21-day cycle until DP or unacceptable toxicity, for a maximum of 6 cycles.

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

Dosage and administration details:

Participants received bevacizumab 15 mg/kg IV infusion on Day 1 of each 21-day cycle until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Investigational medicinal product name	MEGF0444A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants also received MEGF0444A at a fixed dose of 600 mg IV infusion on Day 1 of Cycle 1, followed by subsequent doses of 600 mg every 21 days until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Arm title	Placebo

Arm description:

Participants received paclitaxel 200 mg/m^2 IV infusion on Day 1, carboplatin (at doses to achieve an AUC of 6 mg/mL*min) IV infusion on Day 1, and bevacizumab 15 mg/kg IV infusion on Day 1 of each 21-day cycle. Participants also received placebo matched to MEGF0444A IV infusion on Day 1 of Cycle 1, followed by subsequent placebo administration every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by placebo. Paclitaxel and carboplatin were administered until DP or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and placebo were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Arm type	Placebo
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received paclitaxel 200 mg/m^2 IV infusion on Day 1 of each 21-day cycle until DP or unacceptable toxicity, for a maximum of 6 cycles.

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

Dosage and administration details:

Participants received carboplatin (at doses to achieve an AUC of 6 mg/mL*min) IV infusion on Day 1 of each 21-day cycle until DP or unacceptable toxicity, for a maximum of 6 cycles.

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

Dosage and administration details:

Participants received bevacizumab 15 mg/kg IV infusion on Day 1 of each 21-day cycle until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

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

Dosage and administration details:

Participants received placebo matched to MEGF0444A IV infusion on Day 1 of Cycle 1, followed by subsequent placebo administration every 21 days until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Number of subjects in period 1	MEGF0444A	Placebo
Started	52	52
Treated	52	51
Completed	0	0
Not completed	52	52
Consent withdrawn by subject	1	3
Physician decision	-	1
Randomized not treated	-	1
Death	23	18
Study terminated by sponsor	23	28
Unspecified	4	1
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	MEGF0444A

Reporting group description:

Participants received paclitaxel 200 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1, carboplatin (at doses to achieve an area under the concentration time curve [AUC] of 6 milligrams/milliliter*minute [mg/mL*min]) IV infusion on Day 1, and bevacizumab 15 milligrams per kilogram (mg/kg) IV infusion on Day 1 of each 21-day cycle. Participants also received MEGF0444A at a fixed dose of 600 mg IV infusion on Day 1 of Cycle 1, followed by subsequent doses of 600 mg every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by MEGF0444A. Paclitaxel and carboplatin were administered until disease progression (DP) or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and MEGF0444A were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Reporting group title	Placebo

Reporting group description:

Participants received paclitaxel 200 mg/m^2 IV infusion on Day 1, carboplatin (at doses to achieve an AUC of 6 mg/mL*min) IV infusion on Day 1, and bevacizumab 15 mg/kg IV infusion on Day 1 of each 21-day cycle. Participants also received placebo matched to MEGF0444A IV infusion on Day 1 of Cycle 1, followed by subsequent placebo administration every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by placebo. Paclitaxel and carboplatin were administered until DP or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and placebo were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Reporting group values	MEGF0444A	Placebo	Total
Number of subjects	52	52	104
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	62.9	62.3	
standard deviation	± 8.6	± 9.6	-
Gender categorical Units: Subjects			
Female	19	18	37
Male	33	34	67

End points

End points reporting groups

Reporting group title	MEGF0444A

Reporting group description:

Participants received paclitaxel 200 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1, carboplatin (at doses to achieve an area under the concentration time curve [AUC] of 6 milligrams/milliliter*minute [mg/mL*min]) IV infusion on Day 1, and bevacizumab 15 milligrams per kilogram (mg/kg) IV infusion on Day 1 of each 21-day cycle. Participants also received MEGF0444A at a fixed dose of 600 mg IV infusion on Day 1 of Cycle 1, followed by subsequent doses of 600 mg every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by MEGF0444A. Paclitaxel and carboplatin were administered until disease progression (DP) or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and MEGF0444A were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Reporting group title	Placebo

Reporting group description:

Participants received paclitaxel 200 mg/m^2 IV infusion on Day 1, carboplatin (at doses to achieve an AUC of 6 mg/mL*min) IV infusion on Day 1, and bevacizumab 15 mg/kg IV infusion on Day 1 of each 21-day cycle. Participants also received placebo matched to MEGF0444A IV infusion on Day 1 of Cycle 1, followed by subsequent placebo administration every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by placebo. Paclitaxel and carboplatin were administered until DP or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and placebo were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Primary: Percentage of Participants With Disease Progression (DP) or Death

End point title	Percentage of Participants With Disease Progression (DP) or Death[1]

End point description:

PFS was defined as time from randomization to the first occurrence of documented DP (according to Response Evaluation Criteria in Solid Tumors [RECIST], Version 1.1 [v 1.1]) or death from any cause on study, whichever occurred earlier, as determined by investigator. Death on study is defined as death from any cause within 30 days of last study treatment. Determination of DP for the purpose of treatment decisions and timing of the primary analysis was based on investigator assessment, using RECIST v 1.1. Tumor assessment was performed by RECIST v 1.1. DP was defined as at least a 20 percent (%) 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 millimeter (mm). The appearance of one or more new lesions is also considered progression. Analysis population included all participants who were randomized.

End point type	Primary

End point timeframe:

Baseline up to DP or death, whichever occurred first (assessed at baseline, Day 15 of each cycle [21-day cycles], end of treatment or early termination [up to 24 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 statistical analysis was planned for this outcome.

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Percentage of participants				
number (not applicable)	75	44.2		

Statistical analyses

No statistical analyses for this end point

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as time from randomization to the first occurrence of documented DP (according to RECIST v 1.1) or death from any cause on study, whichever occurred earlier, as determined by investigator. DP was 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 one or more new lesions is also considered progression. Median and the 95% confidence interval (CI) were estimated using Kaplan-Meier survival methodology. Analysis population included all participants who were randomized.

End point type	Primary

End point timeframe:

Baseline up to DP or death, whichever occurred first (assessed at baseline, Day 15 of each cycle [21-day cycles], end of treatment or early termination [up to 24 months])

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Months				
median (confidence interval 95%)	6.7 (5.68 to 7.43)	8.1 (5.88 to 11.14)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The unstratified Cox proportional hazard model was used to estimate the hazard ratio (the magnitude of the treatment effect) and the corresponding 95% CI.

Comparison groups	Placebo v MEGF0444A
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0466
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.686

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.003
upper limit	2.835

Secondary: Percentage of Participants With Objective Response (OR)

End point title	Percentage of Participants With Objective Response (OR)

End point description:

Percentage of participants with OR based assessment of confirmed complete response (CR) or confirmed partial response (PR) as per RECIST v 1.1. Confirmed responses: persist on repeat imaging study at least 4 weeks after initial documentation of response. CR: disappearance of all target and non-target lesions; normalization of tumor markers. Non-pathological lymph nodes: short axis measures less than (<) 10 mm. PR: at least a 30% decrease in sum of diameters of target lesions, taking as reference the baseline sum diameters. DP: at least a 20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study and the sum must also demonstrate absolute increase of at least 5 mm. Appearance of one or more new lesions is also considered progression. Analysis population included all participants who were randomized.

End point type	Secondary

End point timeframe:

Baseline up to DP or death, whichever occurred first (assessed at baseline, Day 15 of each cycle [21-day cycles], end of treatment or early termination [up to 24 months])

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Percentage of participants				
number (not applicable)	28.8	55.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	MEGF0444A v Placebo
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0095
Method	Logrank

Secondary: Duration of Objective Response

End point title	Duration of Objective Response

End point description:

Duration of objective response was defined as the first occurrence of objective response to DP or death due to any cause on study. DP was 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 one or more new lesions is also considered progression. Data not available as the study was terminated because of lack of efficacy of study drug in participants with NSCLC.

End point type	Secondary

End point timeframe:

Baseline up to DP or death, whichever occurred first (assessed at baseline, Day 15 of each cycle [21-day cycles], end of treatment or early termination [up to 24 months])

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - Data not available due to early study termination.

[3] - Data not available due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time from randomization until death from any cause. All deaths were included, without regard to whether they occur on study or following treatment discontinuation. Overall survival was censored at the date of last contact for participants who were alive. Analysis population included all participants who were randomized. The number 99999 signified data not available as the study was terminated because of lack of efficacy of study drug in participants with NSCLC.

End point type	Secondary

End point timeframe:

Baseline until death (assessed at baseline, Day 15 of each cycle [21-day cycles], end of treatment or early termination [up to 24 months], and thereafter every 3 months until death [up to approximately 2.75 years])

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Months				
median (confidence interval 95%)	99999 (9.69 to 99999)	12.4 (11.89 to 12.52)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The unstratified Cox proportional hazard model was used to estimate the hazard ratio (the magnitude of the treatment effect) and the corresponding 95% CI.

Comparison groups	MEGF0444A v Placebo
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8465
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.525
upper limit	2.206

Secondary: Percentage of Participants Who Died

End point title	Percentage of Participants Who Died

End point description:

Analysis population included all participants who were randomized.

End point type	Secondary

End point timeframe:

Baseline until death (assessed at baseline, Day 15 of each cycle [21-day cycles], end of treatment or early termination [up to 24 months], and thereafter every 3 months until death [up to approximately 2.75 years])

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	52		
Units: Percentage of participants				
number (not applicable)	28.8	28.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) Scores

End point title	Change From Baseline in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) Scores

End point description:

EORTC QLQ-C30: included global health status/quality of life (QOL), functional scales (physical, role,

cognitive, emotional, and social), symptom scales (fatigue, pain, nausea/vomiting), and single items (dyspnea, appetite loss, insomnia, constipation, diarrhea, and financial difficulties). Most questions used a 4-point scale (1 'Not at All' to 4 'Very Much'); 2 questions used a 7-point scale (1 'Very Poor' to 7 'Excellent'). Scores were averaged and transformed to 0-100 scale; a higher score for Global QOL/functional scales indicates better level of QOL/functioning, or a higher score for symptom scale indicates greater degree of symptoms. Data not available as the study was terminated because of lack of efficacy of study drug in participants with NSCLC.

End point type	Secondary

End point timeframe:

Baseline up to early termination or end of treatment (up to 24 months)

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Units on a scale				
arithmetic mean (confidence interval 95%)	(to)	(to)		

Notes:

[4] - Data not available due to early study termination.

[5] - Data not available due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EORTC QLQ Lung Cancer Module 13 (LC-13)

End point title	Change From Baseline in EORTC QLQ Lung Cancer Module 13 (LC-13)

End point description:

EORTC QLQ-LC13: consisted of 13 questions with one symptom scale for dyspnea of 3 items and 10 single items (cough, haemoptysis, sore mouth, dysphagia, peripheral neuropathy, alopecia, pain in chest, pain in arm/shoulder, other pain, pain medication). Questions used 4-point scale (1 'Not at all' to 4 'Very much'. Scores were averaged and transformed to 0-100 scale; higher score = greater degree of symptoms. Data not available as the study was terminated because of lack of efficacy of study drug in participants with NSCLC.

End point type	Secondary

End point timeframe:

Baseline up to early termination or end of treatment (up to 24 months)

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Units on a scale				
arithmetic mean (confidence interval 95%)	(to)	(to)		

Notes:

[6] - Data not available due to early study termination.

[7] - Data not available due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Delay in Deterioration of Disease Symptoms of Cough, Dyspnea, Pain

End point title	Delay in Deterioration of Disease Symptoms of Cough, Dyspnea, Pain

End point description:

Delay in deterioration of disease symptoms was defined as time taken for clinically meaningful change (greater than or equal to [>/=] 10 points) in each of the symptoms: cough, dyspnea and pain. Data not available as the study was terminated because of lack of efficacy of study drug in participants with NSCLC.

End point type	Secondary

End point timeframe:

Baseline up to early termination or end of treatment (up to 24 months)

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[8] - Data not available due to early study termination.

[9] - Data not available due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Clinically Meaningful Impact on Global Health Status/QOL and Functional Scales by EORTC QLQ-C30 Improvement Category

End point title	Percentage of Participants With Clinically Meaningful Impact on Global Health Status/QOL and Functional Scales by EORTC QLQ-C30 Improvement Category

End point description:

EORTC QLQ-C30: included global health status/QOL, functional scales (physical, role, cognitive, emotional, and social). Most questions used a 4-point scale (1 'Not at All' to 4 'Very Much'); health status/QOL questions used a 7-point scale (1 'Very Poor' to 7 'Excellent'). Scores were averaged and transformed to 0-100 scale; a higher score for Global QOL/functional scales indicates better level of QOL/functioning. Data not available as the study was terminated because of lack of efficacy of study drug in participants with NSCLC.

End point type	Secondary

End point timeframe:

Baseline up to early termination or end of treatment (up to 24 months)

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: Percentage of participants				
number (not applicable)				

Notes:

[10] - Data not available due to early study termination.

[11] - Data not available due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Clinically Meaningful Treatment-Related Symptoms

End point title	Percentage of Participants With Clinically Meaningful Treatment-Related Symptoms

End point description:

Clinically meaningful treatment-related symptoms was defined as participants reporting "quite a bit" or "very much" symptoms for the symptom scales. Symptom scale (fatigue, pain, nausea/vomiting) scores averaged, transformed to 0-100 scale; higher score=greater degree of symptoms. Data not available as the study was terminated because of lack of efficacy of study drug in participants with NSCLC.

End point type	Secondary

End point timeframe:

Baseline up to early termination or end of treatment (up to 24 months)

End point values	MEGF0444A	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: Percentage of Participants				
number (not applicable)				

Notes:

[12] - Data not available due to early study termination.

[13] - Data not available due to early study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Day 1 Cycle 1) up to end of treatment or early termination (up to 24 months)

Adverse event reporting additional description:

Safety population included all randomized participants who received at least one dose of study treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	MEGF0444A

Reporting group description:

Participants received paclitaxel 200 mg/m^2 IV infusion on Day 1, carboplatin (at doses to achieve an AUC of 6 mg/mL*min] IV infusion on Day 1, and bevacizumab 15 mg/kg IV infusion on Day 1 of each 21-day cycle. Participants also received MEGF0444A at a fixed dose of 600 mg IV infusion on Day 1 of Cycle 1, followed by subsequent doses of 600 mg every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by MEGF0444A. Paclitaxel and carboplatin were administered until DP or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and MEGF0444A were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Reporting group title	Placebo

Reporting group description:

Participants received paclitaxel 200 mg/m^2 IV infusion on Day 1, carboplatin (at doses to achieve an AUC of 6 mg/mL*min) IV infusion on Day 1, and bevacizumab 15 mg/kg IV infusion on Day 1 of each 21-day cycle. Participants also received placebo matched to MEGF0444A IV infusion on Day 1 of Cycle 1, followed by subsequent placebo administration every 21 days. The preferred order of study treatment administration was paclitaxel, carboplatin, and bevacizumab, followed by placebo. Paclitaxel and carboplatin were administered until DP or unacceptable toxicity, for a maximum of 6 cycles; bevacizumab and placebo were administered until DP or unacceptable toxicity, for a maximum of 24 months (34 cycles).

Serious adverse events	MEGF0444A	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 52 (55.77%)	30 / 51 (58.82%)	
number of deaths (all causes)	24	18	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	5 / 52 (9.62%)	4 / 51 (7.84%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 5	0 / 4	
Lung neoplasm malignant			

subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Lung lobectomy			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracotomy			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 52 (1.92%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthenia			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 52 (1.92%)	4 / 51 (7.84%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 52 (3.85%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Aspiration			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cough			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			

subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Inflammatory marker increased			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis radiation			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dizziness			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
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			
Febrile neutropenia			
subjects affected / exposed	3 / 52 (5.77%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Anaemia			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 52 (3.85%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 52 (1.92%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 52 (1.92%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	1 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
subjects affected / exposed	1 / 52 (1.92%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 52 (3.85%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	

Lung abscess			
subjects affected / exposed	0 / 52 (0.00%)	2 / 51 (3.92%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchitis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Febrile infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
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 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 52 (0.00%)	1 / 51 (1.96%)	
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	MEGF0444A	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 52 (96.15%)	49 / 51 (96.08%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 52 (17.31%)	13 / 51 (25.49%)	
occurrences (all)	10	19	
Hypotension			
subjects affected / exposed	2 / 52 (3.85%)	3 / 51 (5.88%)	
occurrences (all)	2	5	
Flushing			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	4	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	17 / 52 (32.69%)	17 / 51 (33.33%)	
occurrences (all)	37	33	
Fatigue			
subjects affected / exposed	24 / 52 (46.15%)	18 / 51 (35.29%)	
occurrences (all)	31	27	
Pyrexia			
subjects affected / exposed	7 / 52 (13.46%)	3 / 51 (5.88%)	
occurrences (all)	9	3	
Chest pain			
subjects affected / exposed	5 / 52 (9.62%)	3 / 51 (5.88%)	
occurrences (all)	5	4	
Mucosal inflammation			
subjects affected / exposed	4 / 52 (7.69%)	4 / 51 (7.84%)	
occurrences (all)	5	4	
Pain			
subjects affected / exposed	5 / 52 (9.62%)	3 / 51 (5.88%)	
occurrences (all)	6	3	
Chills			

subjects affected / exposed	5 / 52 (9.62%)	2 / 51 (3.92%)	
occurrences (all)	6	2	
Oedema Peripheral			
subjects affected / exposed	4 / 52 (7.69%)	2 / 51 (3.92%)	
occurrences (all)	4	3	
Gait disturbance			
subjects affected / exposed	3 / 52 (5.77%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	13 / 52 (25.00%)	13 / 51 (25.49%)	
occurrences (all)	14	16	
Epistaxis			
subjects affected / exposed	13 / 52 (25.00%)	12 / 51 (23.53%)	
occurrences (all)	19	14	
Cough			
subjects affected / exposed	11 / 52 (21.15%)	5 / 51 (9.80%)	
occurrences (all)	12	5	
Oropharyngeal pain			
subjects affected / exposed	4 / 52 (7.69%)	4 / 51 (7.84%)	
occurrences (all)	4	5	
Productive cough			
subjects affected / exposed	5 / 52 (9.62%)	2 / 51 (3.92%)	
occurrences (all)	6	2	
Dysphonia			
subjects affected / exposed	2 / 52 (3.85%)	4 / 51 (7.84%)	
occurrences (all)	2	5	
Haemoptysis			
subjects affected / exposed	4 / 52 (7.69%)	2 / 51 (3.92%)	
occurrences (all)	4	2	
Dyspnoea exertional			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	4	2	
Psychiatric disorders			

Anxiety			
subjects affected / exposed	3 / 52 (5.77%)	8 / 51 (15.69%)	
occurrences (all)	3	8	
Insomnia			
subjects affected / exposed	1 / 52 (1.92%)	12 / 51 (23.53%)	
occurrences (all)	1	12	
Depression			
subjects affected / exposed	2 / 52 (3.85%)	3 / 51 (5.88%)	
occurrences (all)	2	4	
Investigations			
Weight decreased			
subjects affected / exposed	6 / 52 (11.54%)	9 / 51 (17.65%)	
occurrences (all)	7	9	
Neutrophil count decreased			
subjects affected / exposed	1 / 52 (1.92%)	3 / 51 (5.88%)	
occurrences (all)	1	5	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 52 (1.92%)	3 / 51 (5.88%)	
occurrences (all)	1	3	
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	15 / 52 (28.85%)	16 / 51 (31.37%)	
occurrences (all)	21	18	
Peripheral sensory neuropathy			
subjects affected / exposed	6 / 52 (11.54%)	7 / 51 (13.73%)	
occurrences (all)	12	14	
Polyneuropathy			
subjects affected / exposed	8 / 52 (15.38%)	4 / 51 (7.84%)	
occurrences (all)	17	8	
Headache			
subjects affected / exposed	8 / 52 (15.38%)	5 / 51 (9.80%)	
occurrences (all)	16	5	
Dysgeusia			
subjects affected / exposed	2 / 52 (3.85%)	11 / 51 (21.57%)	
occurrences (all)	2	13	

Paraesthesia			
subjects affected / exposed	6 / 52 (11.54%)	3 / 51 (5.88%)	
occurrences (all)	7	7	
Dizziness			
subjects affected / exposed	4 / 52 (7.69%)	6 / 51 (11.76%)	
occurrences (all)	5	7	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	21 / 52 (40.38%)	24 / 51 (47.06%)	
occurrences (all)	45	51	
Thrombocytopenia			
subjects affected / exposed	13 / 52 (25.00%)	20 / 51 (39.22%)	
occurrences (all)	24	37	
Anaemia			
subjects affected / exposed	15 / 52 (28.85%)	16 / 51 (31.37%)	
occurrences (all)	20	27	
Leukopenia			
subjects affected / exposed	3 / 52 (5.77%)	6 / 51 (11.76%)	
occurrences (all)	3	8	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	18 / 52 (34.62%)	24 / 51 (47.06%)	
occurrences (all)	33	39	
Diarrhoea			
subjects affected / exposed	21 / 52 (40.38%)	16 / 51 (31.37%)	
occurrences (all)	41	19	
Constipation			
subjects affected / exposed	18 / 52 (34.62%)	17 / 51 (33.33%)	
occurrences (all)	19	22	
Vomiting			
subjects affected / exposed	9 / 52 (17.31%)	11 / 51 (21.57%)	
occurrences (all)	10	16	
Dyspepsia			
subjects affected / exposed	3 / 52 (5.77%)	5 / 51 (9.80%)	
occurrences (all)	3	5	
Haemorrhoids			

subjects affected / exposed	3 / 52 (5.77%)	5 / 51 (9.80%)	
occurrences (all)	3	5	
Abdominal pain			
subjects affected / exposed	2 / 52 (3.85%)	5 / 51 (9.80%)	
occurrences (all)	2	5	
Abdominal pain upper			
subjects affected / exposed	2 / 52 (3.85%)	4 / 51 (7.84%)	
occurrences (all)	3	5	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	23 / 52 (44.23%)	22 / 51 (43.14%)	
occurrences (all)	25	25	
Rash			
subjects affected / exposed	4 / 52 (7.69%)	6 / 51 (11.76%)	
occurrences (all)	4	8	
Night sweats			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	4	1	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	6 / 52 (11.54%)	5 / 51 (9.80%)	
occurrences (all)	8	8	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 52 (23.08%)	12 / 51 (23.53%)	
occurrences (all)	19	22	
Pain in extremity			
subjects affected / exposed	9 / 52 (17.31%)	9 / 51 (17.65%)	
occurrences (all)	11	12	
Myalgia			
subjects affected / exposed	6 / 52 (11.54%)	11 / 51 (21.57%)	
occurrences (all)	8	12	
Muscular weakness			
subjects affected / exposed	3 / 52 (5.77%)	6 / 51 (11.76%)	
occurrences (all)	3	10	
Muscle spasms			

subjects affected / exposed	5 / 52 (9.62%)	3 / 51 (5.88%)	
occurrences (all)	6	4	
Back pain			
subjects affected / exposed	4 / 52 (7.69%)	3 / 51 (5.88%)	
occurrences (all)	4	5	
Bone pain			
subjects affected / exposed	3 / 52 (5.77%)	3 / 51 (5.88%)	
occurrences (all)	6	3	
Musculoskeletal pain			
subjects affected / exposed	5 / 52 (9.62%)	2 / 51 (3.92%)	
occurrences (all)	7	2	
Musculoskeletal chest pain			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Neck pain			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Spinal pain			
subjects affected / exposed	3 / 52 (5.77%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 52 (7.69%)	2 / 51 (3.92%)	
occurrences (all)	4	4	
Rhinitis			
subjects affected / exposed	4 / 52 (7.69%)	0 / 51 (0.00%)	
occurrences (all)	7	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 52 (3.85%)	4 / 51 (7.84%)	
occurrences (all)	2	5	
Urinary tract infection			
subjects affected / exposed	3 / 52 (5.77%)	2 / 51 (3.92%)	
occurrences (all)	5	2	
Pneumonia			
subjects affected / exposed	4 / 52 (7.69%)	1 / 51 (1.96%)	
occurrences (all)	4	1	

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	20 / 52 (38.46%)	17 / 51 (33.33%)	
occurrences (all)	30	25	
Dehydration			
subjects affected / exposed	6 / 52 (11.54%)	4 / 51 (7.84%)	
occurrences (all)	11	9	
Hypokalaemia			
subjects affected / exposed	4 / 52 (7.69%)	6 / 51 (11.76%)	
occurrences (all)	9	13	
Hypomagnesaemia			
subjects affected / exposed	5 / 52 (9.62%)	4 / 51 (7.84%)	
occurrences (all)	14	7	
Hyponatraemia			
subjects affected / exposed	2 / 52 (3.85%)	6 / 51 (11.76%)	
occurrences (all)	3	7	
Hyperglycaemia			
subjects affected / exposed	0 / 52 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2012	This amendment included study conduct modifications arising from the updated safety experience.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
06 June 2013	The protocol specified primary analysis conducted after the occurrence of approximately 60 PFS events demonstrated no evidence of efficacy with the addition of MEGF0444A to the reference regimen in participants with NSCLC and subsequently the study was terminated by the sponsors.	-

Notes:

Limitations and caveats

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

The study was terminated because of lack of efficacy of study drug in participants with NSCLC.

Notes: