Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Phase 2 Study to Assess the Efficacy and Safety of Farletuzumab (MORAb-003) in Combination with Carboplatin plus Paclitaxel or Carboplatin plus Pegylated Liposomal Doxorubicin (PLD) in Subjects with Low CA125 Platinum-Sensitive Ovarian Cancer

Summary

EudraCT number	2014-003812-36
Trial protocol	BE DE GB ES IT
Global end of trial date	13 August 2020

Results information

Result version number	v1 (current)
This version publication date	25 August 2021
First version publication date	25 August 2021

Trial information

Trial identification

Sponsor protocol code	MORAb-003-011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02289950
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Ltd.
Sponsor organisation address	European Knowledge Centre, Mosquito Way, Hatfield, United Kingdom, AL10 9SN
Public contact	Eisai Medical Information, Eisai Inc., 1 888-274-2378, esi_oncmedinfo@eisai.com
Scientific contact	Eisai Medical Information, Eisai Inc., 1 888-274-2378, esi_oncmedinfo@eisai.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	13 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate that farletuzumab has superior efficacy compared with placebo in improving Progression-free survival (PFS), as determined by Response Evaluation Criteria In Solid Tumors (RECIST) 1.1, when added to the standard chemotherapy regimens of carboplatin plus paclitaxel or carboplatin plus PLD, in subjects with platinum-sensitive ovarian cancer in first relapse who have a cancer antigen 125 (CA125) greater than or equal to (>=) 3 x upper limit of normal (ULN) (105 units per milliliter [U/mL]) at study entry.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following: - Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2013) - International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use - Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312 - European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states. - Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan’s GCP.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2015
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	Belgium: 21
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 35
Country: Number of subjects enrolled	Japan: 22
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 92
Worldwide total number of subjects	214
EEA total number of subjects	96

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)	117
From 65 to 84 years	95
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 60 investigative sites in the United states, Belgium, Germany, Italy, Spain, United Kingdom and Japan from 19 March 2015 to 13 August 2020.

Pre-assignment

Screening details:

A total of 332 subjects were screened, of which 118 were screen failures and 214 were randomized out of which 211 were treated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD

Arm description:

Subjects received either carboplatin (area under the concentration-time curve [AUC] 5) plus paclitaxel 175 milligrams per square meter (mg/m^2) intravenously (IV) every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with farletuzumab loading dose of 10 milligram per kilogram (mg/kg) for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with farletuzumab 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Arm type	Experimental
Investigational medicinal product name	Farletuzumab
Investigational medicinal product code	
Other name	MORAb-003
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Farletuzumab loading dose of 10 mg/kg for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 64 cycles or disease progression.

Arm title	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD

Arm description:

Subjects received either carboplatin (AUC 5) plus paclitaxel 175 mg/m^2 IV every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with placebo loading dose of 10 mg/kg for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with placebo 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Arm type	Placebo

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

Dosage and administration details:

Placebo loading dose of 10 mg/kg for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 64 cycles or disease progression.

Number of subjects in period 1	Farletuzumab 5 mg/kg+Carboplatin/ Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD
Started	142	72
Completed	0	0
Not completed	142	72
Test article held for greater than 28 days	-	1
Physician decision	9	3
Consent withdrawn by subject	1	3
Subject discontinued therapy	9	2
Adverse event, non-fatal	11	3
Other	5	2
Not Treated	2	1
Death	1	1
Progressive disease by RECIST 1.1	99	52
Lost to follow-up	1	-
Progressive disease by Clinical Assessment	4	4

Baseline characteristics

Reporting groups	
Reporting group title	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD

Reporting group description:

Subjects received either carboplatin (area under the concentration-time curve [AUC] 5) plus paclitaxel 175 milligrams per square meter (mg/m^2) intravenously (IV) every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with farletuzumab loading dose of 10 milligram per kilogram (mg/kg) for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with farletuzumab 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Reporting group title	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD

Reporting group description:

Subjects received either carboplatin (AUC 5) plus paclitaxel 175 mg/m^2 IV every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with placebo loading dose of 10 mg/kg for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with placebo 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Reporting group values	Farletuzumab 5 mg/kg+Carboplatin/ Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD	Total
Number of subjects	142	72	214
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	62.0	62.9	
standard deviation	± 10.74	± 10.50	-
Gender Categorical			
Units: Subjects			
Female	141	72	213
Unknown	1	0	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	12	3	15
Not Hispanic or Latino	126	68	194
Unknown or Not Reported	4	1	5
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	14	8	22
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	8	2	10
White	117	62	179

More than one race	0	0	0
Unknown or Not Reported	3	0	3

End points

End points reporting groups

Reporting group title	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD

Reporting group description:

Subjects received either carboplatin (area under the concentration-time curve [AUC] 5) plus paclitaxel 175 milligrams per square meter (mg/m^2) intravenously (IV) every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with farletuzumab loading dose of 10 milligram per kilogram (mg/kg) for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with farletuzumab 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Reporting group title	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD

Reporting group description:

Subjects received either carboplatin (AUC 5) plus paclitaxel 175 mg/m^2 IV every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with placebo loading dose of 10 mg/kg for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with placebo 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Primary: Progression Free Survival (PFS)

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

End point description:

PFS was defined as the time (in months) from the date of randomization of a subject to the date of first observation of progression or date of death, whatever the cause. PFS was assessed based on the investigators' assessments utilizing Response Evaluation Criteria In Solid Tumors (RECIST) 1.1. Disease progression (PD) was defined as at least a 20 percent (%) increase or 5 millimeter (mm) increase in the sum of diameters of target lesions (taking as reference the smallest sum on study) recorded since the treatment started or the appearance of 1 or more new lesions. PFS was estimated and analyzed using Kaplan-Meier method. The intent to treat (ITT) Population (Full Analysis Set) included all randomized subjects according to the assigned treatment by interactive response technology (IRT) system.

End point type	Primary

End point timeframe:

From the date of randomization to the date of first documentation of PD, or date of death, whichever occurs first up to approximately 5 years 5 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	72		
Units: Months				
median (confidence interval 95%)	11.73 (10.22 to 13.60)	10.78 (9.49 to 13.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from the date of randomization until the date of death. Subjects were censored at the date of last known to be alive. OS was analyzed using Kaplan-Meier method. The ITT Population (Full Analysis Set) included all randomized subjects according to the assigned treatment by IRT system. Here '99999' means that the upper limit of 95% confidence interval (CI) was not estimable due to insufficient number of events.

End point type	Secondary

End point timeframe:

From the date of randomization until the date of death (up to approximately 5 years 5 months)

End point values	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	72		
Units: Months				
median (confidence interval 95%)	43.07 (37.13 to 99999)	42.45 (37.85 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Best Overall Response (BOR)

End point title	Number of Subjects With Best Overall Response (BOR)

End point description:

BOR was defined as the best response of complete response (CR) or partial response (PR) or stable disease (SD) for >=6 months recorded from the start of the treatment until PD or death, whichever occurred first based on investigator assessment per RECIST v1.1. CR: disappearance of all target and non-target lesions. All pathological (whether target or non-target) must have a reduction in their short axis <10 mm. PR: at least a 30% decrease in the sum of diameter (SOD) of target lesions, taking as reference the baseline sum diameters. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SOD. PD was defined as at least 20% increase (including an absolute increase of at least 5 mm) in the SOD of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. Tumor Response Evaluable Analysis Set was used.

End point type	Secondary

End point timeframe:

From first dose of study drug (Baseline) up to approximately 5 years 5 months

End point values	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138	68		
Units: Subjects				
Complete Response	24	15		
Partial Response	72	35		
Stable Disease	36	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumor Response (TTR)

End point title	Time to Tumor Response (TTR)

End point description:

TTR was defined as the time (in months) from the date of randomization to the date of first observation of response (PR or CR) (whichever status was recorded first). TTR was assessed based on investigator assessment utilizing RECIST 1.1. CR: disappearance of all target and non-target lesions. All pathological (whether target or non-target) must have a reduction in their short axis <10 mm. PR: at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD. Tumor Response Evaluable Analysis Set included all randomized subjects who received at least 1 dose of study drug and who had a baseline and at least 1 on treatment tumor assessment performed. Here "number of subjects analyzed" signifies subjects who had CR or PR.

End point type	Secondary

End point timeframe:

From the date of randomization until date of first observation of response (CR or PR) up to approximately 5 years 5 months

End point values	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	50		
Units: months				
median (confidence interval 95%)	2.69 (1.74 to 2.83)	2.53 (1.48 to 2.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was defined as the time (in months) from the date of first observation of response (PR or CR) to the date of the first observation of progression based on the investigator's assessment utilizing RECIST 1.1, or date of death, whatever the cause. CR: disappearance of all target and non-target lesions. All pathological (whether target or non-target) must have a reduction in their short axis <10 mm. PR: at least a 30% decrease in the SOD of target lesions, taking as reference the baseline sum diameters. PD was defined as at least 20% increase (including an absolute increase of at least 5 mm) in the SOD of target lesions, taking as reference the smallest sum and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions. Tumor Response Evaluable Analysis Set was used. Here "number of subjects analyzed" signifies subjects who had CR or PR.

End point type	Secondary

End point timeframe:

From date of the first observation of CR or PR until the date of first observation of progression or date of death up to approximately 5 years 5 months

End point values	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	50		
Units: months				
median (confidence interval 95%)	10.12 (8.54 to 11.47)	8.51 (6.31 to 10.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Each Second Platinum-Free Interval Stratified by First Platinum-Free Interval

End point title	Percentage of Subjects Achieving Each Second Platinum-Free Interval Stratified by First Platinum-Free Interval

End point description:

Percentage of Subjects achieving each second platinum-free interval (SPFI) (<6 months, 6-12 months, greater than [>] 12-36 months, and >36 months) stratified by first platinum-free interval (FPFI) (6 to 12 months and >12 to 36 months) was reported. First platinum-free interval was defined as the date of

completion of previous platinum-based chemotherapy until the date of first relapse (that is, first observation of progression). The date of first relapse was the progression date. Second platinum-free interval was defined as the date of completion of platinum-based chemotherapy (last dosing date) during the study until the date of progression or death (or censoring, if applicable).The ITT Population (Full Analysis Set) included all randomized subjects according to the assigned treatment by IRT system.

End point type	Secondary

End point timeframe:

From the date of randomization to the date of first relapse (or first observation of progression/death) up to approximately 5 year 5 months

End point values	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	72		
Units: Percentage of subjects				
number (confidence interval 95%)				
SPFI(<6 months): FPFI(6 to 12 months)	71.2 (57.92 to 82.42)	63.3 (43.86 to 80.07)		
SPFI (6-12 months): FPFI (6 to 12 months)	6.8 (1.88 to 16.46)	23.3 (9.93 to 42.28)		
SPFI(>12-36 months): FPFI(6 to 12 months)	16.9 (8.44 to 28.97)	10.0 (2.11 to 26.53)		
SPFI(>36 months): FPFI (6 to 12 months)	0.0 (0.00 to 6.60)	0.0 (0.00 to 11.57)		
SPFI(<6 months): FPFI(>12 to 36 months)	42.2 (31.40 to 53.51)	52.4 (36.42 to 68.00)		
SPFI(6-12 months): FPFI (>12 to 36 months)	33.7 (23.72 to 44.95)	28.6 (15.72 to 44.58)		
SPFI(>12-36 months): FPFI (>12 to 36 months)	20.5 (12.41 to 30.76)	16.7 (6.97 to 31.36)		
SPFI(>36 months): FPFI(>12 to 36 months)	0.0 (0.00 to 4.35)	0.0 (0.00 to 8.41)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose up to 30 days after the last dose of study treatment (up to approximately 5 years 5 months)

Adverse event reporting additional description:

Deaths that happened anytime during the study (including those during the treatment and after treatment discontinuation) are reported in this section.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD

Reporting group description:

Subjects received either carboplatin (AUC 5) plus paclitaxel 175 mg/m^2 IV every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with placebo loading dose of 10 mg/kg for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with placebo 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Reporting group title	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD

Reporting group description:

Subjects received either carboplatin (area under the concentration-time curve [AUC] 5) plus paclitaxel 175 milligrams per square meter (mg/m^2) intravenously (IV) every 3 weeks or carboplatin (AUC 5) plus PLD 30 mg/m^2 IV every 4 weeks in combination with farletuzumab loading dose of 10 milligram per kilogram (mg/kg) for the first 2 weeks, followed by 5 mg/kg every week thereafter administered up to maximum of 8 cycles at the investigator's discretion. Subjects who completed combination treatment phase and Subjects who experienced intolerable toxicity to chemotherapy in combination treatment phase continued to receive maintenance treatment with farletuzumab 5 mg/kg every week alone up to maximum of 64 cycles or until disease progression was confirmed by radiographic assessment, or subject discontinued treatment for any other reason.

Serious adverse events	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD	Farletuzumab 5 mg/kg+Carboplatin/Paclitaxel or Carboplatin/PLD	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 70 (25.71%)	42 / 141 (29.79%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
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			
Chest pain			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			

subjects affected / exposed	2 / 70 (2.86%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 70 (0.00%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restrictive pulmonary disease			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
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 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 70 (1.43%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
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	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Carbon monoxide diffusing capacity decreased			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 70 (0.00%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Heat illness			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	0 / 70 (0.00%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 70 (1.43%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 70 (1.43%)	6 / 141 (4.26%)	
occurrences causally related to treatment / all	0 / 1	5 / 9	
deaths causally related to treatment / all	0 / 0	1 / 1	
Neutropenia			
subjects affected / exposed	2 / 70 (2.86%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	0 / 70 (0.00%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 70 (2.86%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 70 (2.86%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 70 (1.43%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 70 (0.00%)	3 / 141 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 70 (1.43%)	5 / 141 (3.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 70 (1.43%)	3 / 141 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 70 (1.43%)	7 / 141 (4.96%)	
occurrences causally related to treatment / all	0 / 2	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated umbilical hernia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 70 (2.86%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
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			

Petechiae			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 70 (1.43%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 70 (0.00%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 70 (0.00%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tracheitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 70 (0.00%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 70 (1.43%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 70 (1.43%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	1 / 70 (1.43%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 1	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	Placebo + Carboplatin/Paclitaxel or Carboplatin/PLD	Farletuzumab 5 mg/kg+Carboplatin/ Paclitaxel or Carboplatin/PLD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 70 (100.00%)	140 / 141 (99.29%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	9 / 70 (12.86%)	4 / 141 (2.84%)	
occurrences (all)	17	4	
Hypertension			
subjects affected / exposed	5 / 70 (7.14%)	7 / 141 (4.96%)	
occurrences (all)	14	10	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	14 / 70 (20.00%)	33 / 141 (23.40%)	
occurrences (all)	42	90	
Chills			
subjects affected / exposed	5 / 70 (7.14%)	6 / 141 (4.26%)	
occurrences (all)	5	9	
Influenza like illness			
subjects affected / exposed	4 / 70 (5.71%)	8 / 141 (5.67%)	
occurrences (all)	5	10	
Fatigue			
subjects affected / exposed	35 / 70 (50.00%)	69 / 141 (48.94%)	
occurrences (all)	55	112	
Malaise			
subjects affected / exposed	9 / 70 (12.86%)	9 / 141 (6.38%)	
occurrences (all)	11	14	
Oedema peripheral			

subjects affected / exposed	12 / 70 (17.14%)	16 / 141 (11.35%)	
occurrences (all)	19	21	
Peripheral swelling			
subjects affected / exposed	4 / 70 (5.71%)	4 / 141 (2.84%)	
occurrences (all)	4	4	
Pyrexia			
subjects affected / exposed	11 / 70 (15.71%)	23 / 141 (16.31%)	
occurrences (all)	16	37	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	5 / 70 (7.14%)	4 / 141 (2.84%)	
occurrences (all)	6	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 70 (22.86%)	43 / 141 (30.50%)	
occurrences (all)	25	65	
Dyspnoea			
subjects affected / exposed	9 / 70 (12.86%)	31 / 141 (21.99%)	
occurrences (all)	13	47	
Epistaxis			
subjects affected / exposed	5 / 70 (7.14%)	7 / 141 (4.96%)	
occurrences (all)	7	10	
Nasal congestion			
subjects affected / exposed	2 / 70 (2.86%)	10 / 141 (7.09%)	
occurrences (all)	3	11	
Oropharyngeal pain			
subjects affected / exposed	7 / 70 (10.00%)	16 / 141 (11.35%)	
occurrences (all)	10	18	
Psychiatric disorders			
Depression			
subjects affected / exposed	6 / 70 (8.57%)	6 / 141 (4.26%)	
occurrences (all)	16	6	
Anxiety			
subjects affected / exposed	5 / 70 (7.14%)	15 / 141 (10.64%)	
occurrences (all)	5	18	
Insomnia			

subjects affected / exposed	8 / 70 (11.43%)	15 / 141 (10.64%)	
occurrences (all)	11	17	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 70 (5.71%)	7 / 141 (4.96%)	
occurrences (all)	4	10	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 70 (5.71%)	10 / 141 (7.09%)	
occurrences (all)	4	16	
Neutrophil count decreased			
subjects affected / exposed	18 / 70 (25.71%)	44 / 141 (31.21%)	
occurrences (all)	90	165	
Platelet count decreased			
subjects affected / exposed	11 / 70 (15.71%)	27 / 141 (19.15%)	
occurrences (all)	46	83	
White blood cell count decreased			
subjects affected / exposed	14 / 70 (20.00%)	34 / 141 (24.11%)	
occurrences (all)	68	127	
Nervous system disorders			
Dizziness			
subjects affected / exposed	13 / 70 (18.57%)	22 / 141 (15.60%)	
occurrences (all)	19	40	
Dysgeusia			
subjects affected / exposed	12 / 70 (17.14%)	15 / 141 (10.64%)	
occurrences (all)	17	22	
Headache			
subjects affected / exposed	27 / 70 (38.57%)	49 / 141 (34.75%)	
occurrences (all)	61	77	
Paraesthesia			
subjects affected / exposed	8 / 70 (11.43%)	11 / 141 (7.80%)	
occurrences (all)	13	14	
Peripheral sensory neuropathy			
subjects affected / exposed	14 / 70 (20.00%)	23 / 141 (16.31%)	
occurrences (all)	21	31	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	36 / 70 (51.43%)	76 / 141 (53.90%)	
occurrences (all)	121	208	
Leukopenia			
subjects affected / exposed	7 / 70 (10.00%)	21 / 141 (14.89%)	
occurrences (all)	20	74	
Neutropenia			
subjects affected / exposed	24 / 70 (34.29%)	55 / 141 (39.01%)	
occurrences (all)	82	225	
Thrombocytopenia			
subjects affected / exposed	19 / 70 (27.14%)	42 / 141 (29.79%)	
occurrences (all)	86	109	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	5 / 70 (7.14%)	3 / 141 (2.13%)	
occurrences (all)	5	3	
Vertigo			
subjects affected / exposed	6 / 70 (8.57%)	8 / 141 (5.67%)	
occurrences (all)	9	8	
Eye disorders			
Vision blurred			
subjects affected / exposed	5 / 70 (7.14%)	7 / 141 (4.96%)	
occurrences (all)	5	7	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	9 / 70 (12.86%)	9 / 141 (6.38%)	
occurrences (all)	11	14	
Abdominal distension			
subjects affected / exposed	4 / 70 (5.71%)	9 / 141 (6.38%)	
occurrences (all)	5	12	
Abdominal pain upper			
subjects affected / exposed	12 / 70 (17.14%)	17 / 141 (12.06%)	
occurrences (all)	17	19	
Abdominal pain			
subjects affected / exposed	22 / 70 (31.43%)	39 / 141 (27.66%)	
occurrences (all)	34	65	
Constipation			

subjects affected / exposed	31 / 70 (44.29%)	58 / 141 (41.13%)	
occurrences (all)	53	93	
Diarrhoea			
subjects affected / exposed	27 / 70 (38.57%)	48 / 141 (34.04%)	
occurrences (all)	63	83	
Dry mouth			
subjects affected / exposed	6 / 70 (8.57%)	9 / 141 (6.38%)	
occurrences (all)	8	9	
Dyspepsia			
subjects affected / exposed	10 / 70 (14.29%)	12 / 141 (8.51%)	
occurrences (all)	14	15	
Nausea			
subjects affected / exposed	45 / 70 (64.29%)	95 / 141 (67.38%)	
occurrences (all)	110	187	
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 70 (7.14%)	12 / 141 (8.51%)	
occurrences (all)	6	18	
Stomatitis			
subjects affected / exposed	24 / 70 (34.29%)	44 / 141 (31.21%)	
occurrences (all)	51	66	
Vomiting			
subjects affected / exposed	27 / 70 (38.57%)	43 / 141 (30.50%)	
occurrences (all)	56	74	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	15 / 70 (21.43%)	26 / 141 (18.44%)	
occurrences (all)	19	29	
Blister			
subjects affected / exposed	4 / 70 (5.71%)	0 / 141 (0.00%)	
occurrences (all)	5	0	
Erythema			
subjects affected / exposed	4 / 70 (5.71%)	9 / 141 (6.38%)	
occurrences (all)	4	9	
Dry skin			
subjects affected / exposed	9 / 70 (12.86%)	4 / 141 (2.84%)	
occurrences (all)	10	5	

Nail discolouration			
subjects affected / exposed	4 / 70 (5.71%)	4 / 141 (2.84%)	
occurrences (all)	4	4	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	9 / 70 (12.86%)	11 / 141 (7.80%)	
occurrences (all)	13	13	
Pruritus			
subjects affected / exposed	9 / 70 (12.86%)	15 / 141 (10.64%)	
occurrences (all)	14	17	
Rash			
subjects affected / exposed	13 / 70 (18.57%)	24 / 141 (17.02%)	
occurrences (all)	15	38	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	4 / 70 (5.71%)	11 / 141 (7.80%)	
occurrences (all)	5	16	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	15 / 70 (21.43%)	36 / 141 (25.53%)	
occurrences (all)	27	52	
Arthritis			
subjects affected / exposed	5 / 70 (7.14%)	1 / 141 (0.71%)	
occurrences (all)	6	1	
Back pain			
subjects affected / exposed	18 / 70 (25.71%)	18 / 141 (12.77%)	
occurrences (all)	24	24	
Bone pain			
subjects affected / exposed	4 / 70 (5.71%)	6 / 141 (4.26%)	
occurrences (all)	7	10	
Flank pain			
subjects affected / exposed	4 / 70 (5.71%)	3 / 141 (2.13%)	
occurrences (all)	4	3	
Muscle spasms			
subjects affected / exposed	11 / 70 (15.71%)	8 / 141 (5.67%)	
occurrences (all)	17	9	
Muscular weakness			

subjects affected / exposed	4 / 70 (5.71%)	3 / 141 (2.13%)	
occurrences (all)	4	5	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 70 (1.43%)	9 / 141 (6.38%)	
occurrences (all)	1	11	
Musculoskeletal pain			
subjects affected / exposed	6 / 70 (8.57%)	13 / 141 (9.22%)	
occurrences (all)	6	15	
Myalgia			
subjects affected / exposed	7 / 70 (10.00%)	15 / 141 (10.64%)	
occurrences (all)	13	19	
Neck pain			
subjects affected / exposed	4 / 70 (5.71%)	6 / 141 (4.26%)	
occurrences (all)	6	7	
Pain in extremity			
subjects affected / exposed	12 / 70 (17.14%)	17 / 141 (12.06%)	
occurrences (all)	18	22	
Infections and infestations			
Cystitis			
subjects affected / exposed	4 / 70 (5.71%)	6 / 141 (4.26%)	
occurrences (all)	5	9	
Influenza			
subjects affected / exposed	7 / 70 (10.00%)	9 / 141 (6.38%)	
occurrences (all)	9	12	
Nasopharyngitis			
subjects affected / exposed	14 / 70 (20.00%)	22 / 141 (15.60%)	
occurrences (all)	26	34	
Sinusitis			
subjects affected / exposed	8 / 70 (11.43%)	10 / 141 (7.09%)	
occurrences (all)	11	11	
Upper respiratory tract infection			
subjects affected / exposed	6 / 70 (8.57%)	23 / 141 (16.31%)	
occurrences (all)	8	29	
Urinary tract infection			
subjects affected / exposed	16 / 70 (22.86%)	18 / 141 (12.77%)	
occurrences (all)	32	24	

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	18 / 70 (25.71%)	28 / 141 (19.86%)	
occurrences (all)	32	43	
Dehydration			
subjects affected / exposed	7 / 70 (10.00%)	13 / 141 (9.22%)	
occurrences (all)	8	21	
Hyperglycaemia			
subjects affected / exposed	6 / 70 (8.57%)	7 / 141 (4.96%)	
occurrences (all)	6	18	
Hypertriglyceridaemia			
subjects affected / exposed	4 / 70 (5.71%)	7 / 141 (4.96%)	
occurrences (all)	4	12	
Hypokalaemia			
subjects affected / exposed	4 / 70 (5.71%)	23 / 141 (16.31%)	
occurrences (all)	9	49	
Hypomagnesaemia			
subjects affected / exposed	7 / 70 (10.00%)	21 / 141 (14.89%)	
occurrences (all)	11	33	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2015	The protocol was amended to add method of randomization, updated Inclusion Criteria and exclusion criteria, clarified stopping rules for the study, added urine pregnancy testing (to be conducted locally), specified that the censoring and handling rules on missing values will be detailed in the statistical analysis plan, as well as potential sensitivity analyses with regard to missing values and updated quantities of blood to be drawn for bioanalytical sampling to more closely align with central laboratory blood sample handling practices, statement instructing sites to send images to central imaging laboratory for rapid reads in the case of suspected disease progression was removed and removal of reference to subject initials on the Investigational Product accountability log as only subject number will be captured.
18 December 2017	The protocol was amended to remove the 1:1 target stratification ratio and the associated minimum enrollment of 105 subjects per stratum and the description of the required number PFS events, sample size considerations were no longer based on the effect of farletuzumab on PFS in each of the 2 chemotherapy regimens, changed assumption for median PFS to 11 months in the control arm, changed assumption for median OS to 32 months, removed the description of the secondary efficacy analyses to be conducted in both strata, added that the primary and secondary analyses (PFS, OS, ORR, DR) in each strata were to be considered as exploratory analyses, revised inclusion and exclusion criteria and added that the alpha allocation between the interim and final OS analyses will be determined based on the Lan-DeMets spending function with O'Brien-Fleming boundary.
06 November 2018	The protocol was amended to replace "Morphotek" with "Eisai" to update study ownership.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported