Clinical trial results:
A Randomized, Open-Label Phase 2 Study of EC145 Single-agent and the Combination of EC145 plus Docetaxel Versus Docetaxel Alone in Participants with Folate-Receptor Positive [FR(++)] Second Line NSCLC

Summary

EudraCT number	2012-000966-40
Trial protocol	HU CZ ES GB BG DE
Global end of trial date	01 June 2015

Results information

Result version number	v1 (current)
This version publication date	23 August 2018
First version publication date	23 August 2018
Summary attachment (see zip file)	EC-FV-07 CSR (FEB-2017) (EC-FV-07 CSR Synopsis (FEB-2017).pdf)

Trial information

Trial identification

Sponsor protocol code	EC-FV-07

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01577654
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Endocyte, Inc.
Sponsor organisation address	3000 Kent Avenue, Suite A1-100, West Lafayette, United States, 47906
Public contact	Christopher Jordan, Endocyte, Inc., +1 3176080769, cjordan@endocyte.com
Scientific contact	Christopher Jordan, Endocyte, Inc., +1 3176080769, cjordan@endocyte.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	14 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 February 2014
Global end of trial reached?	Yes
Global end of trial date	01 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study tests the activity of single-agent EC145 and the combination of EC145 plus docetaxel against the current standard docetaxel in second line NSCLC in participants with all target lesions expressing the folate receptor [FR(++)]. Primary objective: progression free survival (PFS)

Protection of trial subjects:

Preparation of the ICF is the responsibility of the investigator and must include all elements required by the International Conference on Harmonization (ICH), Good Clinical Practice (GCP), Health Insurance Portability and Accountability Act (HIPAA) or other local regulatory requirements for protection of personal information, and other applicable regulatory requirements and must adhere to the ethical principles that have their origin in the Declaration of Helsinki. The ICF will be approved and reviewed by the sponsor prior to IRB/IEC review.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	20 April 2012
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	Poland: 17
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Bulgaria: 13
Country: Number of subjects enrolled	Czech Republic: 5
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Hungary: 36
Country: Number of subjects enrolled	United States: 35
Country: Number of subjects enrolled	Romania: 31
Country: Number of subjects enrolled	Russian Federation: 29
Worldwide total number of subjects	199
EEA total number of subjects	135

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)	109
From 65 to 84 years	90
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A randomized trial was proposed to minimize patient and/or investigator bias. The differences in treatment schedules and anticipated differences in toxicity made an open-label study more pragmatic than a blinded study. The multicenter design of the study provided reassurance that the study population would include a broad variety of patients.

Pre-assignment

Screening details:

Medical history, physical examination, and ECOG; Radiographic analysis - target lesions identified within 28 days prior to first dose of study treatment and prior to imaging; Pregnancy test for all women of childbearing age; Hematology, serum chemistry, and urinalysis; Imaging for eligibility determination; Documentation of concomitant medications.

Pre-assignment period milestones

Number of subjects started	336[1]
Intermediate milestone: Number of subjects	Received EC20: 290
Intermediate milestone: Number of subjects	Randomized: 203
Number of subjects completed	199

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Did not meet inclusion criteria: 133
Reason: Number of subjects	Consent withdrawn by subject: 2
Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Physician decision: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number enrolled includes only those subjects who completed the trial whereas the pre-assignment period begins with the total number of subjects screened.

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-label study

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental: Arm A: EC145 Alone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	EC145
Investigational medicinal product code	
Other name	Vintafolide
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Vintafolide was administered as a 2.5 mg IV bolus injection on Days 1, 4, 8, and 11 during Weeks 1 and 2 of a 3-week cycle.

Investigational medicinal product name	EC20
Investigational medicinal product code	
Other name	Etarfolatide
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Prior to SPECT imaging, patients received 1 IV injection of 0.5 mg folic acid, 1 to 3 minutes before a 1 to 2 mL
IV injection of 0.1 mg etarfolatide labeled with 20 mCi to 25 mCi of 99mTc.

Arm title	Experimental: Arm B: EC145 + Docetaxel

Arm description: -

Arm type	Experimental
Investigational medicinal product name	EC145
Investigational medicinal product code	
Other name	Vintafolide
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Vintafolide was administered as a 2.5 mg IV bolus injection on Days 1, 4, 8, and 11 during Weeks 1 and 2 of a 3-week cycle.

Investigational medicinal product name	EC20
Investigational medicinal product code	
Other name	Etarfolatide
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Prior to SPECT imaging, patients received 1 IV injection of 0.5 mg folic acid, 1 to 3 minutes before a 1 to 2 mL
IV injection of 0.1 mg etarfolatide labeled with 20 mCi to 25 mCi of 99mTc.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel was administered at 75 mg/m2 IV over 1 hour on Day 1 of a 3-week cycle; must have been in conjunction with Day 1 of vintafolide administration for patients in the combination treatment arm. All patients receiving docetaxel were to be pre-medicated with oral dexamethasone according to standard medical practice unless medically contraindicated: 16 mg per day for 3 days starting 1 day prior to docetaxel administration.

Arm title	Active Comparator: Arm C: Docetaxel Alone

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel was administered at 75 mg/m2 IV over 1 hour on Day 1 of a 3-week cycle; must have been in conjunction with Day 1 of vintafolide administration for patients in the combination treatment arm. All patients receiving docetaxel were to be pre-medicated with oral dexamethasone according to standard

medical practice unless medically contraindicated: 16 mg per day for 3 days starting 1 day prior to docetaxel administration.

Investigational medicinal product name	EC20
Investigational medicinal product code	
Other name	Etarfolatide
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Prior to SPECT imaging, patients received 1 IV injection of 0.5 mg folic acid, 1 to 3 minutes before a 1 to 2 mL
IV injection of 0.1 mg etarfolatide labeled with 20 mCi to 25 mCi of 99mTc.

Number of subjects in period 1	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone
Started	63	68	68
Completed	63	68	68

Baseline characteristics

Reporting groups	
Reporting group title	Experimental: Arm A: EC145 Alone
Reporting group description: -	
Reporting group title	Experimental: Arm B: EC145 + Docetaxel
Reporting group description: -	
Reporting group title	Active Comparator: Arm C: Docetaxel Alone
Reporting group description: -	

Reporting group values	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone
Number of subjects	63	68	68
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	32	36	41
From 65-84 years	31	32	27
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	18	21	16
Male	45	47	52
Race Units: Subjects			
Asian	0	1	2
Black/African American	0	1	1
White	60	65	63
Missing	3	1	2
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	59	67	66
Missing	3	1	2
ECOG performance status Units: Subjects			
00	14	18	18
01	48	50	50
02	1	0	0
Smoking Status Units: Subjects			
Never smoked	15	7	10

Formerly smoked	29	43	37
Currently smoke	19	18	21
Type of Cancer Units: Subjects			
Adenocarcinoma	37	39	43
Adenosquamous carcinoma	2	2	5
Adenocarcinoma with other NSCLC variants	2	2	1
Squamous cell carcinoma	22	25	19
Time since last chemotherapy Units: Subjects			
<3 months	31	33	34
>3 months	32	35	34
Best response to last chemotherapy Units: Subjects			
CR/PR/SD	46	49	48
PD/Unknown	17	19	20
Disease stage Units: Subjects			
Stage IIIB	12	10	9
Stage IV	51	58	59
Prior treatment with EGFR inhibitor Units: Subjects			
Yes	11	10	9
No	52	58	59

Reporting group values	Total		
Number of subjects	199		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	109		
From 65-84 years	90		
85 years and over	0		
Gender categorical Units: Subjects			
Female	55		
Male	144		
Race Units: Subjects			
Asian	3		
Black/African American	2		
White	188		
Missing	6		
Ethnicity			

Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	192		
Missing	6		
ECOG performance status Units: Subjects			
00	50		
01	148		
02	1		
Smoking Status Units: Subjects			
Never smoked	32		
Formerly smoked	109		
Currently smoke	58		
Type of Cancer Units: Subjects			
Adenocarcinoma	119		
Adenosquamous carcinoma	9		
Adenocarcinoma with other NSCLC variants	5		
Squamous cell carcinoma	66		
Time since last chemotherapy Units: Subjects			
<3 months	98		
>3 months	101		
Best response to last chemotherapy Units: Subjects			
CR/PR/SD	143		
PD/Unknown	56		
Disease stage Units: Subjects			
Stage IIIB	31		
Stage IV	168		
Prior treatment with EGFR inhibitor Units: Subjects			
Yes	30		
No	169		

End points

End points reporting groups

Reporting group title	Experimental: Arm A: EC145 Alone
Reporting group description: -	
Reporting group title	Experimental: Arm B: EC145 + Docetaxel
Reporting group description: -	
Reporting group title	Active Comparator: Arm C: Docetaxel Alone
Reporting group description: -	
Subject analysis set title	Efficacy Analysis Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The efficacy analysis population consisted of all randomized patients who received 1 or more doses of vintafolide and/or docetaxel, by planned treatment.	
Subject analysis set title	Safety Analysis Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety analysis population consisted of all randomized patients who received at least 1 dose of vintafolide and/or docetaxel, by actual treatment.	

Primary: PFS

End point title	PFS
End point description:	
End point type	Primary
End point timeframe:	
31 May 2012 - 14 February 2014	

End point values	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	68	68	
Units: Months				
median (confidence interval 95%)	1.6 (1.4 to 3.2)	4.2 (2.8 to 5.4)	3.3 (1.7 to 4.2)	

Statistical analyses

Statistical analysis title	Efficacy Analysis
Comparison groups	Experimental: Arm B: EC145 + Docetaxel v Active Comparator: Arm C: Docetaxel Alone v Experimental: Arm A: EC145 Alone

Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1
Method	Logrank

Secondary: Overall Response Rate

End point title	Overall Response Rate

End point description:

End point type	Secondary

End point timeframe:

31 May 2012 - 14 February 2014

End point values	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	68	68	
Units: ORR	4	15	9	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate

End point title	Disease Control Rate

End point description:

End point type	Secondary

End point timeframe:

31 May 2012 - 14 February 2014

End point values	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	68	68	
Units: DCR	26	48	41	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Disease Controls

End point title	Duration of Disease Controls

End point description:

End point type	Secondary

End point timeframe:

31 May 2012 - 14 February 2014

End point values	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	68	68	
Units: Months				
median (confidence interval 95%)	4.3 (3.2 to 5.1)	5.4 (4.2 to 6.1)	5.5 (4.1 to 6.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

31 May 2012 - 14 February 2014

End point values	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	68	68	
Units: Months				
median (confidence interval 95%)	8.4 (5.6 to 12.3)	11.5 (7.3 to 12.9)	8.8 (5.4 to 12.7)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 31 May 2012-14 February 2014	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15
Reporting groups	
Reporting group title	Experimental: Arm A: EC145 Alone
Reporting group description: -	
Reporting group title	Experimental: Arm B: EC145 + Docetaxel
Reporting group description: -	
Reporting group title	Active Comparator: Arm C: Docetaxel Alone
Reporting group description: -	

Serious adverse events	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 63 (22.22%)	29 / 68 (42.65%)	24 / 68 (35.29%)
number of deaths (all causes)	31	27	34
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Non-small cell lung cancer			
subjects affected / exposed	1 / 63 (1.59%)	0 / 68 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 63 (1.59%)	2 / 68 (2.94%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Circulatory collapse			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Embolism			

subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	1 / 27	0 / 34
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	1 / 27	0 / 34
Cardiac failure acute			
subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	1 / 27	0 / 34
Cardiac failure congestive			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Nervous system disorders			
Brain compression			
subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	1 / 27	0 / 34
Hemiparesis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 63 (0.00%)	8 / 68 (11.76%)	4 / 68 (5.88%)
occurrences causally related to treatment / all	0 / 12	8 / 12	4 / 12
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Neutropenia			
subjects affected / exposed	0 / 63 (0.00%)	8 / 68 (11.76%)	3 / 68 (4.41%)
occurrences causally related to treatment / all	0 / 11	8 / 11	3 / 11
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34

Anaemia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	3 / 68 (4.41%)
occurrences causally related to treatment / all	0 / 4	0 / 4	2 / 4
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 63 (0.00%)	2 / 68 (2.94%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 2
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 5	4 / 5	0 / 5
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	3 / 63 (4.76%)	2 / 68 (2.94%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 6	0 / 6	0 / 6
deaths causally related to treatment / all	3 / 31	0 / 27	1 / 34
Pleural effusion			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	2 / 68 (2.94%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Pulmonary embolism			
subjects affected / exposed	0 / 63 (0.00%)	2 / 68 (2.94%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Acute lung injury			

subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Aspiration			
subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	1 / 27	0 / 34
Respiratory arrest			
subjects affected / exposed	1 / 63 (1.59%)	0 / 68 (0.00%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 31	0 / 27	0 / 34
Respiratory distress			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Respiratory failure			
subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	1 / 27	0 / 34
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	2 / 68 (2.94%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Neutropenic sepsis			
subjects affected / exposed	0 / 63 (0.00%)	3 / 68 (4.41%)	0 / 68 (0.00%)
occurrences causally related to treatment / all	0 / 3	3 / 3	0 / 3
deaths causally related to treatment / all	0 / 31	1 / 27	0 / 34

Sepsis			
subjects affected / exposed	0 / 63 (0.00%)	2 / 68 (2.94%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 3	2 / 3	0 / 3
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34
Pneumonia bacterial			
subjects affected / exposed	0 / 63 (0.00%)	0 / 68 (0.00%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 31	0 / 27	1 / 34
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 63 (0.00%)	3 / 68 (4.41%)	1 / 68 (1.47%)
occurrences causally related to treatment / all	0 / 4	2 / 4	1 / 4
deaths causally related to treatment / all	0 / 31	0 / 27	0 / 34

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

Non-serious adverse events	Experimental: Arm A: EC145 Alone	Experimental: Arm B: EC145 + Docetaxel	Active Comparator: Arm C: Docetaxel Alone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 63 (85.71%)	67 / 68 (98.53%)	65 / 68 (95.59%)
Investigations			
Weight decreased			
subjects affected / exposed	2 / 63 (3.17%)	7 / 68 (10.29%)	6 / 68 (8.82%)
occurrences (all)	15	15	15
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 63 (1.59%)	4 / 68 (5.88%)	2 / 68 (2.94%)
occurrences (all)	7	7	7
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	10 / 63 (15.87%)	20 / 68 (29.41%)	13 / 68 (19.12%)
occurrences (all)	43	43	43
Headache			
subjects affected / exposed	4 / 63 (6.35%)	3 / 68 (4.41%)	5 / 68 (7.35%)
occurrences (all)	12	12	12
Dizziness			

subjects affected / exposed	2 / 63 (3.17%)	5 / 68 (7.35%)	3 / 68 (4.41%)
occurrences (all)	10	10	10
Dysgeusia			
subjects affected / exposed	0 / 63 (0.00%)	1 / 68 (1.47%)	5 / 68 (7.35%)
occurrences (all)	6	6	6
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 63 (3.17%)	50 / 68 (73.53%)	40 / 68 (58.82%)
occurrences (all)	92	92	92
Anaemia			
subjects affected / exposed	15 / 63 (23.81%)	14 / 68 (20.59%)	20 / 68 (29.41%)
occurrences (all)	49	49	49
Leukopenia			
subjects affected / exposed	1 / 63 (1.59%)	17 / 68 (25.00%)	21 / 68 (30.88%)
occurrences (all)	39	39	39
Febrile Neutropenia			
subjects affected / exposed	0 / 63 (0.00%)	9 / 68 (13.24%)	4 / 68 (5.88%)
occurrences (all)	13	13	13
Thrombocytopenia			
subjects affected / exposed	0 / 63 (0.00%)	5 / 68 (7.35%)	3 / 68 (4.41%)
occurrences (all)	8	8	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 63 (14.29%)	18 / 68 (26.47%)	23 / 68 (33.82%)
occurrences (all)	50	50	50
Asthenia			
subjects affected / exposed	10 / 63 (15.87%)	17 / 68 (25.00%)	9 / 68 (13.24%)
occurrences (all)	36	36	36
Pyrexia			
subjects affected / exposed	0 / 63 (0.00%)	11 / 68 (16.18%)	7 / 68 (10.29%)
occurrences (all)	18	18	18
Chest pain			
subjects affected / exposed	3 / 63 (4.76%)	6 / 68 (8.82%)	1 / 68 (1.47%)
occurrences (all)	10	10	10
Oedema peripheral			

subjects affected / exposed	2 / 63 (3.17%)	5 / 68 (7.35%)	2 / 68 (2.94%)
occurrences (all)	9	9	9
Chills			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	1 / 68 (1.47%)
occurrences (all)	5	5	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 63 (3.17%)	16 / 68 (23.53%)	16 / 68 (23.53%)
occurrences (all)	34	34	34
Nausea			
subjects affected / exposed	3 / 63 (4.76%)	10 / 68 (14.71%)	13 / 68 (19.12%)
occurrences (all)	26	26	26
Stomatitis			
subjects affected / exposed	2 / 63 (3.17%)	13 / 68 (19.12%)	11 / 68 (16.18%)
occurrences (all)	26	26	26
Constipation			
subjects affected / exposed	10 / 63 (15.87%)	6 / 68 (8.82%)	5 / 68 (7.35%)
occurrences (all)	21	21	21
Vomiting			
subjects affected / exposed	3 / 63 (4.76%)	9 / 68 (13.24%)	8 / 68 (11.76%)
occurrences (all)	20	20	20
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	7 / 63 (11.11%)	7 / 68 (10.29%)	11 / 68 (16.18%)
occurrences (all)	25	25	25
Cough			
subjects affected / exposed	3 / 63 (4.76%)	5 / 68 (7.35%)	5 / 68 (7.35%)
occurrences (all)	13	13	13
Haemoptysis			
subjects affected / exposed	6 / 63 (9.52%)	3 / 68 (4.41%)	3 / 68 (4.41%)
occurrences (all)	12	12	12
Hypoxia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	0 / 68 (0.00%)
occurrences (all)	4	4	4
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	0 / 63 (0.00%)	11 / 68 (16.18%)	13 / 68 (19.12%)
occurrences (all)	24	24	24
Rash			
subjects affected / exposed	0 / 63 (0.00%)	6 / 68 (8.82%)	3 / 68 (4.41%)
occurrences (all)	9	9	9
Dry skin			
subjects affected / exposed	1 / 63 (1.59%)	4 / 68 (5.88%)	0 / 68 (0.00%)
occurrences (all)	5	5	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 63 (7.94%)	8 / 68 (11.76%)	10 / 68 (14.71%)
occurrences (all)	23	23	23
Myalgia			
subjects affected / exposed	3 / 63 (4.76%)	8 / 68 (11.76%)	7 / 68 (10.29%)
occurrences (all)	18	18	18
Back pain			
subjects affected / exposed	0 / 63 (0.00%)	5 / 68 (7.35%)	7 / 68 (10.29%)
occurrences (all)	12	12	12
Pain in extremity			
subjects affected / exposed	2 / 63 (3.17%)	5 / 68 (7.35%)	4 / 68 (5.88%)
occurrences (all)	11	11	11
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	2 / 68 (2.94%)
occurrences (all)	6	6	6
Oral candidiasis			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	0 / 68 (0.00%)
occurrences (all)	4	4	4
Respiratory tract infection			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	0 / 68 (0.00%)
occurrences (all)	4	4	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 63 (14.29%)	14 / 68 (20.59%)	11 / 68 (16.18%)
occurrences (all)	34	34	34

Dehydration			
subjects affected / exposed	1 / 63 (1.59%)	6 / 68 (8.82%)	4 / 68 (5.88%)
occurrences (all)	11	11	11
Hypokalaemia			
subjects affected / exposed	1 / 63 (1.59%)	8 / 68 (11.76%)	1 / 68 (1.47%)
occurrences (all)	10	10	10
Hyponatraemia			
subjects affected / exposed	0 / 63 (0.00%)	8 / 68 (11.76%)	2 / 68 (2.94%)
occurrences (all)	10	10	10
Hyperglycaemia			
subjects affected / exposed	0 / 63 (0.00%)	5 / 68 (7.35%)	4 / 68 (5.88%)
occurrences (all)	9	9	9
Hypomagnesaemia			
subjects affected / exposed	0 / 63 (0.00%)	6 / 68 (8.82%)	1 / 68 (1.47%)
occurrences (all)	7	7	7
Hypoalbuminaemia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 68 (5.88%)	2 / 68 (2.94%)
occurrences (all)	6	6	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported