



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 ^{99m}Tc.

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

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