# Clinical trial results:
# Estudio fase III, multicéntrico, abierto, randomizado de tratamiento con erlotinib (Tarceva®) versus quimioterapia en pacientes con carcinoma no microcítico de pulmón avanzado que presentan mutaciones en el dominio tirosina quinasa (TK) del Receptor del Factor de Crecimiento Epidérmico (EGFR)

# A phase III, multicenter, open-label, randomized trial of erlotinib (Tarceva®) versus chemotherapy in patients with advanced non-small cell lung cancer with mutations in the tyrosine kinase domain of the Epidermal Growth Factor Receptor (EGFR)

## Summary

| | |
|---|---|
| EudraCT number | 2006-003568-73 |
| Trial protocol | FR IT ES |
| Global end of trial date | 11 April 2022 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 22 February 2025 |
| First version publication date | 22 February 2025 |
| Summary attachment (see zip file) | Lancet Oncol article_EURTAC (Rosell_Erlotinib_EURTAC.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | GECP06/01 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00446225 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Spanish Lung Cancer Group |
| Sponsor organisation address | Avda. Meridiana 358; 6th floor, Barcelona, Spain, 08027 |
| Public contact | Eva Pereira, Spanish Lung Cancer Group, 34 93 4302006, epereira@gecp.org |
| Scientific contact | Eva Pereira, Spanish Lung Cancer Group, 34 93 4302006, epereira@gecp.org |

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 | 11 April 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 11 April 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 April 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Comparar la supervivencia libre de progresión, evaluada por el investigador, en los dos brazos de tratamiento del estudio (quimioterapia convencional versus erlotinib) en pacientes con cáncer de pulmón no microcítico (CPNM) en estadios avanzados (estadio IIIB y estadio IV), que no han recibido quimioterapia previa para su enfermedad y que presentan mutaciones en el dominio tirosina quinasa del receptor del factor de crecimiento epidérmico (EGFR).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 15 February 2007 |
| 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 | Spain: 115 |
| Country: Number of subjects enrolled | France: 39 |
| Country: Number of subjects enrolled | Italy: 19 |
| Worldwide total number of subjects | 173 |
| EEA total number of subjects | 173 |

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) | 86 |
| From 65 to 84 years | 87 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Between Feb 15, 2007, and Jan 4, 2011, 174 patients with EGFR mutations were enrolled in the study from 42 hospitals in France, Italy, and Spain.

### Pre-assignment

Screening details:

Screening details: Eligible participants were adults (>18 years) with NSCLC and EGFR mutations (exon 19 deletion or L858R mutation in
exon 21) with no history of chemotherapy for metastatic disease (neoadjuvant or adjuvant chemotherapy ending ≥6 months
before study entry was allowed).

### Period 1

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

Blinding implementation details:

Not Blinded

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Experimental: Erlotinib |

Arm description:

Erlotinib (Tarceva)150 mg /day

Patients will receive treatment until disease progression or unacceptable toxicity.

For all practical effects a treatment cycle will be defined as three weeks of continuous treatment with erlotinib

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Erlotinib |
| Investigational medicinal product code | |
| Other name | Tarceva |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Erlotinib (Tarceva)150 mg /day

For all practical effects a treatment cycle will be defined as three weeks of continuous treatment with erlotinib
These tablets are typically taken once a day, with or without food

Patients will receive treatment until disease progression or unacceptable toxicity.

| | |
|---|---|
| **Arm title** | Control: Standard Chemotherapy Group |

Arm description:

4 cycles of Chemotherapy:
Cisplatin / Gemcitabine;
Cisplatin /Docetaxel;
Carboplatin / Gemcitabine;
Carboplatin / Docetaxel.

3 week cycles of standard intravenous chemotherapy
-75 mg/m² cisplatin plus 75 mg/m² docetaxel on day 1 or

-75 mg/m² cisplatin on day 1 plus 1250 mg/m² gemcitabine on days 1 and 8

Patients who were ineligible for cisplatin treatment received intra venous carboplatin chemotherapy instead:
-3 week cycles of carboplatin AUC 6 on day 1 with 75 mg/m² docetaxel on day 1 or
-3 week cycles carboplatin AUC 5 on day 1 with 1000 mg/m² gemcitabine on days 1 and 8

Patients in the chemotherapy arm will receive the treatment until disease progression or unacceptable toxicity occurs, or until a maximum of 4 treatment cycles are given.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | Paraplatin |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Gemcitabine 1000 mg/m2 days 1 and 8 and Carboplatin AUC = 5 day 1, every 21 days.

Docetaxel (75 mg/m2) /carboplatin (AUC=6); Gemcitabine (1000 mg/m2; day 1 and 8) / Carboplatin (AUC=5)

Repeat cycles every 3 weeks.

Patients in the chemotherapy arm will receive the treatment until disease progression or unacceptable toxicity occurs, or until a maximum of 4 treatment cycles are given.

| | |
|---|---|
| Investigational medicinal product name | Gemcitabin |
| Investigational medicinal product code | |
| Other name | Gemzar |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cisplatin (75 mg/m2) / Gemcitabine (1250 mg/m2; day 1 and 8)
Repeat cycles every 3 weeks.
Patients in the chemotherapy arm will receive the treatment until disease progression or unacceptable toxicity occurs, or until a maximum of 4 treatment cycles are given.

| | |
|---|---|
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | Taxotere |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cisplatin (75 mg/m2) / Docetaxel (75 mg/m2)
Repeat cycles every 3 weeks.
Patients in the chemotherapy arm will receive the treatment until disease progression or unacceptable toxicity occurs, or until a maximum of 4 treatment cycles are given.

| | |
|---|---|
| Investigational medicinal product name | Cisplatin |
| Investigational medicinal product code | |
| Other name | Platinol |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

- Cisplatin plus docetaxel: cisplatin 75 mg/m2 i.v. day 1 and docetaxel 75 mg/m2 i.v. day 1. Repeat cycles every 3 weeks.

- Cisplatin plus gemcitabine: Cisplatin 75 mg/m2 i.v. on day 1 and gemcitabine 1250 mg/m2 on days 1 and 8. Repeat cycles every 3 weeks.

Patients in the chemotherapy arm will receive the treatment until disease progression or unacceptable toxicity occurs, or until a maximum of 4 treatment cycles are given.

| **Number of subjects in period 1** | Experimental: Erlotinib | Control: Standard Chemotherapy Group |
|---|---|---|
| Started | 86 | 87 |
| Completed | 86 | 87 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Experimental: Erlotinib |
| Reporting group description: | |
| Erlotinib (Tarceva)150 mg /day<br><br>Patients will receive treatment until disease progression or unacceptable toxicity.<br><br>For all practical effects a treatment cycle will be defined as three weeks of continuous treatment with erlotinib | |
| Reporting group title | Control: Standard Chemotherapy Group |
| Reporting group description: | |
| 4 cycles of Chemotherapy:<br>Cisplatin / Gemcitabine;<br>Cisplatin /Docetaxel;<br>Carboplatin / Gemcitabine;<br>Carboplatin / Docetaxel.<br><br>3 week cycles of standard intravenous chemotherapy<br>-75 mg/m² cisplatin plus 75 mg/m² docetaxel on day 1 or<br>-75 mg/m² cisplatin on day 1 plus 1250 mg/m² gemcitabine on days 1 and 8<br><br>Patients who were ineligible for cisplatin treatment received intra venous carboplatin chemotherapy instead:<br>-3 week cycles of carboplatin AUC 6 on day 1 with 75 mg/m² docetaxel on day 1 or<br>-3 week cycles carboplatin AUC 5 on day 1 with 1000 mg/m² gemcitabine on days 1 and 8<br><br>Patients in the chemotherapy arm will receive the treatment until disease progression or unacceptable toxicity occurs, or until a maximum of 4 treatment cycles are given. | |

| **Reporting group values** | Experimental: Erlotinib | Control: Standard Chemotherapy Group | Total |
|---|---|---|---|
| Number of subjects | 86 | 87 | 173 |
| Age categorical<br>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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous<br>Units: years | | | |
| median | 65 | 65 | |
| full range (min-max) | 53 to 82 | 46 to 82 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 58 | 68 | 126 |
| Male | 28 | 19 | 47 |

| | | | |
|---|---|---|---|
| Race (NIH/OMB)<br>Units: Subjects | | | |
| White | 86 | 85 | 171 |
| Not recorded | 0 | 2 | 2 |
| Smoking status<br>Units: Subjects | | | |
| Never smoked | 57 | 63 | 120 |
| Previous smoker | 22 | 12 | 34 |
| Current smoker | 7 | 12 | 19 |
| ECOG Performance Status Scale<br>Units: Subjects | | | |
| ECOG 0 | 27 | 30 | 57 |
| ECOG 1 | 47 | 45 | 92 |
| ECOG 2 | 12 | 12 | 24 |
| Clinical stage<br>Units: Subjects | | | |
| Stage IIIA | 1 | 0 | 1 |
| Stage IIIB | 6 | 5 | 11 |
| Stage IV | 78 | 82 | 160 |
| Stage IIIC | 1 | 0 | 1 |
| Bone metastasis<br>Units: Subjects | | | |
| Yes | 9 | 11 | 20 |
| No | 77 | 76 | 153 |
| Brain metastasis<br>Units: Subjects | | | |
| Yes | 9 | 11 | 20 |
| No | 77 | 76 | 153 |
| Type of EGFR mutation<br>Units: Subjects | | | |
| Deletion of exon 19 | 57 | 58 | 115 |
| L858R mutation in exon 21 | 29 | 29 | 58 |

## End points

### End points reporting groups

| Reporting group title | Experimental: Erlotinib |
|---|---|

Reporting group description:

Erlotinib (Tarceva)150 mg /day

Patients will receive treatment until disease progression or unacceptable toxicity.

For all practical effects a treatment cycle will be defined as three weeks of continuous treatment with erlotinib

| Reporting group title | Control: Standard Chemotherapy Group |
|---|---|

Reporting group description:

4 cycles of Chemotherapy:
Cisplatin / Gemcitabine;
Cisplatin /Docetaxel;
Carboplatin / Gemcitabine;
Carboplatin / Docetaxel.

3 week cycles of standard intravenous chemotherapy
-75 mg/m² cisplatin plus 75 mg/m² docetaxel on day 1 or
-75 mg/m² cisplatin on day 1 plus 1250 mg/m² gemcitabine on days 1 and 8

Patients who were ineligible for cisplatin treatment received intra venous carboplatin chemotherapy instead:
-3 week cycles of carboplatin AUC 6 on day 1 with 75 mg/m² docetaxel on day 1 or
-3 week cycles carboplatin AUC 5 on day 1 with 1000 mg/m² gemcitabine on days 1 and 8

Patients in the chemotherapy arm will receive the treatment until disease progression or unacceptable toxicity occurs, or until a maximum of 4 treatment cycles are given.

### Primary: Progression Free Survival

| End point title | Progression Free Survival |
|---|---|

End point description:

The time from enrollment in the study to tumor progression or death from any cause (whichever occurs first)

| End point type | Primary |
|---|---|

End point timeframe:

From the date of randomization to the date of last follow up, assessed up to 24 months

| End point values | Experimental: Erlotinib | Control: Standard Chemotherapy Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 9.4 (7.9 to 12.3) | 5.2 (4.4 to 5.8) | | |

## Statistical analyses

| **Statistical analysis title** | PFS between groups |
|---|---|
| Comparison groups | Experimental: Erlotinib v Control: Standard Chemotherapy Group |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.27 |
| upper limit | 0.64 |

## Secondary: Objective Response

| End point title | Objective Response |
|---|---|

End point description:

The objective response is defined as the numbr of patients who attain complete response (CR) or partial response (PR); response will be evaluated following RECIST criteria version 1.0.
Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0) for target lesions and assessed by MRI: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions; Progressive disease (PD): at least a 20% increase in the sum of diameters of target lesions. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD taking as reference the smallest sum of diameters recorded on study.

| End point type | Secondary |
|---|---|

End point timeframe:

From the date of randomization to the date of last follow up, assessed up to 24 months

| **End point values** | Experimental: Erlotinib | Control: Standard Chemotherapy Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: Participant | | | | |
| Complete Response (CR) | 2 | 0 | | |
| Partial Response (PR) | 54 | 14 | | |
| Stable Disease (SD) | 16 | 43 | | |

| | | | | |
|---|---|---|---|---|
| Progressive Disease (PD) | 6 | 11 | | |
| Missing (No Response Assessment) | 8 | 19 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival

| | |
|---|---|
| End point title | Overall survival |

End point description:

Overall Survival (OS) is defined as the time, in months, from the inclusion date to the death date. A patient is censored at the last contact date if he/she does not die.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

From the date of randomization to the date of last follow up, assessed up to 24 months

| End point values | Experimental: Erlotinib | Control: Standard Chemotherapy Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: month | | | | |
| median (confidence interval 95%) | 33.4 (26.7 to 39) | 29.9 (25 to 32.1) | | |

### Statistical analyses

| Statistical analysis title | Overall Survival |
|---|---|
| Comparison groups | Experimental: Erlotinib v Control: Standard Chemotherapy Group |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.043 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.36 |
| upper limit | 0.99 |

## Secondary: Serum EGFR Mutation Status

| End point title | Serum EGFR Mutation Status |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

At baseline

| End point values | Experimental: Erlotinib | Control: Standard Chemotherapy Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 87 | | |
| Units: Sample of serum | | | | |
| Mutated | 30 | 29 | | |
| Wild type | 24 | 23 | | |
| Not enough sample | 2 | 2 | | |
| Not sample | 30 | 33 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the date of randomization until 100 days after last dose of study treatment, assessed up to 36 months.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 6.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Erlotinib Group |
| Reporting group description: - | |
| Reporting group title | Standard chemotherapy group |

Reporting group description: -

| Serious adverse events | Erlotinib Group | Standard chemotherapy group | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 27 / 86 (31.40%) | 25 / 87 (28.74%) | |
| number of deaths (all causes) | 55 | 54 | |
| number of deaths resulting from adverse events | 1 | 2 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastasic pain | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| 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 | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 87 (2.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 86 (3.49%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 2 / 87 (2.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Aplasia cutis congenita | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac tamponade | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 2 / 87 (2.30%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 5 / 87 (5.75%) | |
| occurrences causally related to treatment / all | 0 / 0 | 5 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 3 / 87 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal toxicity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sigmoiditis | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 86 (1.16%) | 3 / 87 (3.45%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 86 (2.33%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 87 (1.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 0 / 87 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Erlotinib Group | Standard chemotherapy group | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 82 / 86 (95.35%) | 81 / 87 (93.10%) | |
| Nervous system disorders | | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 8 / 86 (9.30%) | 12 / 87 (13.79%) | |
| occurrences (all) | 8 | 12 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 48 / 86 (55.81%) | 59 / 87 (67.82%) | |
| occurrences (all) | 48 | 59 | |
| Appetite loss | | | |
| subjects affected / exposed | 26 / 86 (30.23%) | 28 / 87 (32.18%) | |
| occurrences (all) | 26 | 28 | |
| Anaemia | | | |
| subjects affected / exposed | 10 / 86 (11.63%) | 40 / 87 (45.98%) | |
| occurrences (all) | 10 | 40 | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | 27 / 87 (31.03%) | |
| occurrences (all) | 0 | 27 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | 7 / 87 (8.05%) | |
| occurrences (all) | 1 | 7 | |
| Aminotransferase rise | | | |
| subjects affected / exposed | 5 / 86 (5.81%) | 5 / 87 (5.75%) | |
| occurrences (all) | 5 | 5 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 48 / 86 (55.81%) | 15 / 87 (17.24%) | |
| occurrences (all) | 48 | 15 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 86 (1.16%) | 1 / 87 (1.15%) | |
| occurrences (all) | 1 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 67 / 86 (77.91%) | 4 / 87 (4.60%) | |
| occurrences (all) | 67 | 4 | |
| Alopecia | | | |
| subjects affected / exposed | 12 / 86 (13.95%) | 15 / 87 (17.24%) | |
| occurrences (all) | 12 | 15 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 9 / 86 (10.47%) | 5 / 87 (5.75%) | |
| occurrences (all) | 9 | 5 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 26 December 2006 | Adjust the dose of cisplatin when combined with gemcitabine to the standard dose in the clinical practice and modifiy selection criteria, modify secondary objectives. |
| 09 June 2008 | Incorporate the participation of an external evaluator of the imaging tests used for the assessment of the tumor response to the study treatment and Incorporate the participation of two more countries and unify the versions existing in the participating countries. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/22285168