



## 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
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#### 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
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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  $\geq 6$  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
<b>Arm title</b>	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.

<b>Arm title</b>	Control: Standard Chemotherapy Group
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Arm description:

4 cycles of Chemotherapy:

Cisplatin / Gemcitabine;

Cisplatin /Docetaxel;

Carboplatin / Gemcitabine;

Carboplatin / Docetaxel.

3 week cycles of standard intravenous chemotherapy

-75 mg/m<sup>2</sup> cisplatin plus 75 mg/m<sup>2</sup> docetaxel on day 1 or

-75 mg/m<sup>2</sup> cisplatin on day 1 plus 1250 mg/m<sup>2</sup> 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/m<sup>2</sup> docetaxel on day 1 or

-3 week cycles carboplatin AUC 5 on day 1 with 1000 mg/m<sup>2</sup> 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/m<sup>2</sup> days 1 and 8 and Carboplatin AUC = 5 day 1, every 21 days.

Docetaxel (75 mg/m<sup>2</sup>) /carboplatin (AUC=6); Gemcitabine (1000 mg/m<sup>2</sup>; 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/m<sup>2</sup>) / Gemcitabine (1250 mg/m<sup>2</sup>; 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/m<sup>2</sup>) / Docetaxel (75 mg/m<sup>2</sup>)

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/m<sup>2</sup> i.v. day 1 and docetaxel 75 mg/m<sup>2</sup> i.v. day 1. Repeat cycles every 3 weeks.

- Cisplatin plus gemcitabine: Cisplatin 75 mg/m<sup>2</sup> i.v. on day 1 and gemcitabine 1250 mg/m<sup>2</sup> 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
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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
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Reporting group description:

4 cycles of Chemotherapy:

Cisplatin / Gemcitabine;

Cisplatin /Docetaxel;

Carboplatin / Gemcitabine;

Carboplatin / Docetaxel.

3 week cycles of standard intravenous chemotherapy

-75 mg/m<sup>2</sup> cisplatin plus 75 mg/m<sup>2</sup> docetaxel on day 1 or

-75 mg/m<sup>2</sup> cisplatin on day 1 plus 1250 mg/m<sup>2</sup> 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/m<sup>2</sup> docetaxel on day 1 or

-3 week cycles carboplatin AUC 5 on day 1 with 1000 mg/m<sup>2</sup> 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.

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

Race (NIH/OMB)			
Units: Subjects			
White	86	85	171
Not recorded	0	2	2
Smoking status			
Units: Subjects			
Never smoked	57	63	120
Previous smoker	22	12	34
Current smoker	7	12	19
ECOG Performance Status Scale			
Units: Subjects			
ECOG 0	27	30	57
ECOG 1	47	45	92
ECOG 2	12	12	24
Clinical stage			
Units: Subjects			
Stage IIIA	1	0	1
Stage IIIB	6	5	11
Stage IV	78	82	160
Stage IIIC	1	0	1
Bone metastasis			
Units: Subjects			
Yes	9	11	20
No	77	76	153
Brain metastasis			
Units: Subjects			
Yes	9	11	20
No	77	76	153
Type of EGFR mutation			
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
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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/m<sup>2</sup> cisplatin plus 75 mg/m<sup>2</sup> docetaxel on day 1 or

-75 mg/m<sup>2</sup> cisplatin on day 1 plus 1250 mg/m<sup>2</sup> 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/m<sup>2</sup> docetaxel on day 1 or

-3 week cycles carboplatin AUC 5 on day 1 with 1000 mg/m<sup>2</sup> 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
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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
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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

<b>Statistical analysis title</b>	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), $\geq 30\%$ 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	

<b>End point values</b>	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
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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
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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

<b>Statistical analysis title</b>	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

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**Secondary: Serum EGFR Mutation Status**

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End point title	Serum EGFR Mutation Status
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End point description:

End point type	Secondary
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End point timeframe:

At baseline

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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		

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**Statistical analyses**

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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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	6.0
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### Reporting groups

Reporting group title	Erlotinib Group
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Reporting group description: -

Reporting group title	Standard chemotherapy group
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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)			
Metastatic 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 %

<b>Non-serious adverse events</b>	<b>Erlotinib Group</b>	<b>Standard chemotherapy group</b>	
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 occurrences (all)	1 / 86 (1.16%) 1	1 / 87 (1.15%) 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 modify 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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

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