



Clinical trial results:

A Study to Assess the Incidence of Mutations in the Tyrosine Kinase Domain of the Epidermal Growth Factor Receptor in UK Patients with Newly Diagnosed Locally Advanced or Metastatic Non-Small Cell Lung Cancer and to Investigate the Quality of Life of These Patients Undergoing First-Line Monotherapy with Erlotinib (Tarceva®).

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2010-021120-96 |
| Trial protocol | GB |
| Global end of trial date | 07 May 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 25 February 2016 |
| First version publication date | 25 February 2016 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | ML25279 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01250119 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, CH-4070, Basel, Switzerland, |
| Public contact | Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact | Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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 July 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 May 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the prevalence of Epidermal Growth Factor Receptor (EGFR) exon 19 deletion or exon 21 mutation in Non-Small Cell Lung Cancer (NSCLC) participants tested in the United Kingdom (UK).

Protection of trial subjects:

The study was conducted in full conformance with the principles of the Declaration of Helsinki. The study also adhered to the principles outlined in the Guideline for Good Clinical Practice (GCP) International Conference on Harmonisation (ICH) Tripartite Guideline (January 1977) and with local UK law. The investigators ensured compliance with the European Union (EU) Clinical Trial Directive (2001/20/EC).

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment | 19 May 2011 |
| 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 | United Kingdom: 688 |
| Worldwide total number of subjects | 688 |
| EEA total number of subjects | 688 |

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) | 243 |
| From 65 to 84 years | 424 |
| 85 years and over | 21 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the Diagnostic Phase, Screening period was from Day -28 to Day -14 and during the Treatment Phase, Screening period was from Day -14 to Day -1.

Period 1

| | |
|------------------------------|------------------|
| Period 1 title | Diagnostic Phase |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|------------------------------------------|
| Arm title | Non-Small-Cell Lung Cancer (NSCLC) Group |
|------------------|------------------------------------------|

Arm description:

During the Diagnostic Phase participants newly diagnosed with recurrent or metastatic NSCLC were tested for Epidermal Growth Factor Receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.

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

Dosage and administration details:

Erlotinib was administered on an outpatient basis at a fixed dose of 150 mg as a single daily oral dose.

| Number of subjects in period 1 | Non-Small-Cell Lung Cancer (NSCLC) Group |
|----------------------------------|------------------------------------------|
| Started | 688 |
| Completed | 575 |
| Not completed | 113 |
| Participants not tested | 44 |
| Failed to produce a test results | 69 |

Period 2

| | |
|------------------------------|-----------------|
| Period 2 title | Treatment Phase |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|-------------------------------------------|
| Arm title | Erlotinib 150 milligrams per day (mg/day) |
|------------------|-------------------------------------------|

Arm description:

During the Treatment Phase participants found to have a tumor with EGFR exon 19 deletion or exon 21 (L858R) mutations received erlotinib 150 mg/day as a single oral dose until progressive disease (PD), death, unacceptable toxicity or withdrawal of consent.

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

Dosage and administration details:

Erlotinib was administered on an outpatient basis at a fixed dose of 150 mg as a single daily oral dose.

| Number of subjects in period 2^[1] | Erlotinib 150 milligrams per day (mg/day) |
|-----------------------------------------------------|-------------------------------------------|
| Started | 41 |
| Completed | 0 |
| Not completed | 41 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | 2 |
| Unknown reason | 4 |
| Progressive disease | 32 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: During the first period (Diagnostic Phase) participants were tested to determine the presence of EGFR exon 19 deletions or exon 21 (L858R) mutations. Only participants who tested positive for exon 19 deletions or exon 21 (L858R) mutations were included in the second period (Treatment Phase). Out of 52 participants with positive EGFR mutation test result, only 41 participants were treated.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------------------------------|
| Reporting group title | Non-Small-Cell Lung Cancer (NSCLC) Group |
|-----------------------|------------------------------------------|

Reporting group description:

During the Diagnostic Phase participants newly diagnosed with recurrent or metastatic NSCLC were tested for Epidermal Growth Factor Receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.

| Reporting group values | Non-Small-Cell Lung Cancer (NSCLC) Group | Total | |
|-------------------------------------------------------------------------|------------------------------------------|-------|--|
| Number of subjects | 688 | 688 | |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 68 ± 10 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 299 | 299 | |
| Male | 389 | 389 | |

End points

End points reporting groups

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| Reporting group title | Non-Small-Cell Lung Cancer (NSCLC) Group |
| Reporting group description: | |
| During the Diagnostic Phase participants newly diagnosed with recurrent or metastatic NSCLC were tested for Epidermal Growth Factor Receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations. | |
| Reporting group title | Erlotinib 150 milligrams per day (mg/day) |
| Reporting group description: | |
| During the Treatment Phase participants found to have a tumor with EGFR exon 19 deletion or exon 21 (L858R) mutations received erlotinib 150 mg/day as a single oral dose until progressive disease (PD), death, unacceptable toxicity or withdrawal of consent. | |
| Subject analysis set title | EGFR Positive |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All participants who tested positive for EGFR mutations were included in this group. | |
| Subject analysis set title | EGFR Negative |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All participants who tested negative for EGFR mutations were included in this group. | |
| Subject analysis set title | EGFR Positive and Negative |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants who tested either positive or negative for EGFR mutations were included in this group. | |

Primary: Percentage of Participants Who Tested Positive for EGFR Mutations

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| End point title | Percentage of Participants Who Tested Positive for EGFR Mutations ^[1] |
| End point description: | |
| All participants newly diagnosed with recurrent or metastatic NSCLC were tested for EGFR exon 19 deletion or exon 21 mutations. Diagnostic population: All participants newly diagnosed with recurrent or metastatic NSCLC who entered the study and signed the consent form were included in this population. | |
| End point type | Primary |
| End point timeframe: | |
| 14 days | |
| Notes: | |
| [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. | |
| Justification: The primary endpoint in this study was to determine the percentage of participants who test positive for EGFR mutations in the diagnostic phase. Therefore only descriptive analyses were performed for this endpoint. | |

| | | | | |
|-----------------------------------|------------------------------------------|--|--|--|
| End point values | Non-Small-Cell Lung Cancer (NSCLC) Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 644 ^[2] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 8.1 | | | |

Notes:

[2] - Only participants who were tested for EGFR mutations were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With EGFR Mutations by Subgroup

| | |
|-----------------|------------------------------------------------------------|
| End point title | Percentage of Participants With EGFR Mutations by Subgroup |
|-----------------|------------------------------------------------------------|

End point description:

Incidence of EGFR mutations were summarized overall and with respect to different subgroups as follows: (1) equals (=) Histopathology, (2) = Stage of disease, (3) = Age at consent, (4) = Gender, (5) = Race, (6) = Smoking history. Only participants with a valid EGFR mutations test result were included in the analysis. Analysis was performed on the Diagnostic Population.

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

End point timeframe:

14 days

| End point values | EGFR Positive | EGFR Negative | | |
|-----------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 52 | 523 | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| (1) Squamous cell carcinoma | 0 | 22.6 | | |
| (1) Adenocarcinoma | 100 | 67.3 | | |
| (1) Bronchoalveolar carcinoma | 0 | 1.7 | | |
| (1) Large cell carcinoma | 0 | 0.6 | | |
| (1) Other | 0 | 7.8 | | |
| (2) Unresectable Stage IIIB | 1.9 | 11.9 | | |
| (2) Stage IIIB with malignant effusions | 1.9 | 3.4 | | |
| (2) Stage IV | 96.2 | 84.7 | | |
| (3) Less than 70 years | 73.1 | 55.6 | | |
| (3) Greater than 70 years | 26.9 | 44.4 | | |
| (4) Male | 23.1 | 60.8 | | |
| (4) Female | 76.9 | 39.2 | | |
| (5) Asian | 13.5 | 2.9 | | |
| (5) Black | 9.6 | 3.3 | | |
| (5) Caucasian | 75 | 93.5 | | |
| (5) Other | 1.9 | 0.4 | | |
| (6) Never smoked | 44.2 | 7.8 | | |
| (6) Previous smoker | 44.2 | 60.6 | | |
| (6) Current smoker | 7.7 | 31 | | |
| (6) Missing | 3.8 | 0.6 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

| | |
|-------------------|-------------------------------|
| Comparison groups | EGFR Positive v EGFR Negative |
|-------------------|-------------------------------|

| | |
|-----------------------------------------|--------------------|
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0 ^[3] |
| Method | Wald Test |

Notes:

[3] - Test for difference in incidence of EGFR mutations for each subgroup controlled for histopathology; Univariate analysis

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1038 ^[4] |
| Method | Wald Test |

Notes:

[4] - Test for difference in incidence of EGFR mutations for each subgroup controlled for histopathology; Multivariate analysis (6 main effects only).

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 3 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0588 ^[5] |
| Method | Wald Test |

Notes:

[5] - Test for difference in incidence of EGFR mutations for each subgroup controlled for stage of disease; Univariate analysis

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 4 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.4802 ^[6] |
| Method | Wald Test |

Notes:

[6] - Test for difference in incidence of EGFR mutations for each subgroup controlled for stage of disease; Multivariate analysis (6 main effects only).

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 5 |
| Comparison groups | EGFR Negative v EGFR Positive |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0147 ^[7] |
| Method | Wald Test |

Notes:

[7] - Test for difference in incidence of EGFR mutations for each subgroup controlled for age at consent; Multivariate analysis (6 main effects only).

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 6 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1181 ^[8] |
| Method | Wald Test |

Notes:

[8] - Test for difference in incidence of EGFR mutations for each subgroup controlled for age at consent; Multivariate analysis (6 main effects only).

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 7 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0 ^[9] |
| Method | Wald Test |

Notes:

[9] - Test for difference in incidence of EGFR mutations for each subgroup controlled for gender; Univariate analysis.

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 8 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0006 ^[10] |
| Method | Wald Test |

Notes:

[10] - Test for difference in incidence of EGFR mutations for each subgroup controlled for gender; Multivariate analysis (6 main effects only).

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 9 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0004 ^[11] |
| Method | Wald Test |

Notes:

[11] - Test for difference in incidence of EGFR mutations for each subgroup controlled for race; Univariate analysis.

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 10 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3371 ^[12] |
| Method | Wald Test |

Notes:

[12] - Test for difference in incidence of EGFR mutations for each subgroup controlled for race; Multivariate analysis (6 main effects only).

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 11 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0 ^[13] |
| Method | Wald Test |

Notes:

[13] - Test for difference in incidence of EGFR mutations for each subgroup controlled for smoking history; Univariate analysis.

| | |
|-----------------------------------------|-------------------------------|
| Statistical analysis title | Statistical Analysis 12 |
| Comparison groups | EGFR Positive v EGFR Negative |
| Number of subjects included in analysis | 575 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0001 ^[14] |
| Method | Wald Test |

Notes:

[14] - Test for difference in incidence of EGFR mutations for each subgroup controlled for smoking history; Multivariate analysis (6 main effects only).

Secondary: Percentage of Participants With a Response by Best Objective Tumor Response

| | |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Percentage of Participants With a Response by Best Objective Tumor Response |
|-----------------|-----------------------------------------------------------------------------|

End point description:

Best objective response was defined as the best response recorded from the start of treatment until disease progression/recurrence. Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<)10 millimeters (mm). Partial Response (PR): At least a 30 percent (%) decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this may include the baseline sum). The sum must also demonstrate an absolute increase of at least 5 mm. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Intention-to-treat (ITT) population: All participants in the target population who were eligible for treatment and who actually received one dose of treatment.

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

End point timeframe:

Screening, Day 1 of each 6 week visit starting from Visit 3 until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

| | | | | |
|-----------------------------------|-------------------------------------------|--|--|--|
| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| CR | 0 | | | |

| | | | | |
|----|------|--|--|--|
| PR | 84.8 | | | |
| SD | 9.1 | | | |
| PD | 6.1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Probability of Being Alive and Free of Progression by Timepoint

| | |
|-----------------|-----------------------------------------------------------------|
| End point title | Probability of Being Alive and Free of Progression by Timepoint |
|-----------------|-----------------------------------------------------------------|

End point description:

Progression Free Survival (PFS) was defined as the interval (number of days) from the trial treatment start date to the earlier of the date of the first tumor response assessment of PD or the date of death by any cause. Participants who experienced neither of these events or who were lost to followup at the time of the analysis were censored at date of last contact. PFS was summarized according to the Kaplan-Meier method. Analysis was performed on the ITT Population.

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

End point timeframe:

Months 0, 3, 6, 9, 12, 15, and 18

| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
|-----------------------------------|-------------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 ^[15] | | | |
| Units: Probability of being alive | | | | |
| number (confidence interval 95%) | | | | |
| 0 Months | 1 (1 to 1) | | | |
| 3 Months | 0.97 (0.81 to 1) | | | |
| 6 Months | 0.94 (0.78 to 0.98) | | | |
| 9 Months | 0.73 (0.54 to 0.85) | | | |
| 12 Months | 0.54 (0.36 to 0.69) | | | |
| 15 Months | 0.37 (0.21 to 0.54) | | | |
| 18 Months | 0.22 (0.09 to 0.39) | | | |

Notes:

[15] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Survival Time in Months

| | |
|-----------------|-------------------------|
| End point title | Survival Time in Months |
|-----------------|-------------------------|

End point description:

Duration of time in months from Screening until Death due to any cause. Analysis was performed on the ITT population.

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

End point timeframe:

Baseline, Day 1 of each 6-week visit starting from Visit 3 until PD, Death, Unacceptable toxicity or Withdrawal of consent

| | | | | |
|----------------------------------|-------------------------------------------|--|--|--|
| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 12.57 (10.1 to 16.53) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessment Using EuroQol(EQ) 5D Visual Analog Score (VAS) Instrument

| | |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Quality of Life Assessment Using EuroQol(EQ) 5D Visual Analog Score (VAS) Instrument |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The EQ-5D also contains a visual analog scale (EQ-VAS), which records the respondent's self-rated health status on a vertical graduated visual analog scale in millimeters (mm) ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). Analysis was performed on the ITT population.

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

End point timeframe:

Screening, Baseline and Final or Withdrawal Visit up to 34 months

| | | | | |
|----------------------------------------|-------------------------------------------|--|--|--|
| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 40 ^[16] | | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | | | | |
| Screening (n=40) | 62.6 (± 23.5) | | | |
| Baseline (n=20) | 65.4 (± 19.9) | | | |
| Final visit/Withdrawal (n=20) | 63 (± 22.4) | | | |
| Change from Baseline Final visit(n=20) | -0.4 (± 22) | | | |

Notes:

[16] - number (n) = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Problems With Mobility as Assessed Using the EQ-5D

| | |
|-----------------|------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Problems With Mobility as Assessed Using the EQ-5D |
|-----------------|------------------------------------------------------------------------------------|

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their mobility as the following categories: Category 1. I have no problems in walking about; Category 2. I have some problems in walking about; Category 3. I am confined to bed. Analysis was performed on the ITT Population.

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

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
|-----------------------------------|-------------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 ^[17] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Screening Category 1 (n=41) | 43.9 | | | |
| Screening Category 2 (n=41) | 56.1 | | | |
| Screening Category 3 (n=41) | 0 | | | |
| Visit 01 Category 1 (n=20) | 45 | | | |
| Visit 01 Category 2 (n=20) | 55 | | | |
| Visit 01 Category 3 (n=20) | 0 | | | |
| Visit 02 Category 1 (n=33) | 45.5 | | | |
| Visit 02 Category 2 (n=33) | 54.5 | | | |
| Visit 02 Category 3 (n=33) | 0 | | | |
| Visit 03 Category 1 (n=30) | 56.7 | | | |
| Visit 03 Category 2 (n=30) | 43.3 | | | |
| Visit 03 Category 3 (n=30) | 0 | | | |
| Visit 04 Category 1 (n=29) | 51.7 | | | |
| Visit 04 Category 2 (n=29) | 48.3 | | | |
| Visit 04 Category 3 (n=29) | 0 | | | |
| Visit 05 Category 1 (n=33) | 54.5 | | | |
| Visit 05 Category 2 (n=33) | 45.5 | | | |
| Visit 05 Category 3 (n=33) | 0 | | | |
| Visit 06 Category 1 (n=31) | 54.8 | | | |

| | | | | |
|----------------------------|------|--|--|--|
| Visit 06 Category 2 (n=31) | 45.2 | | | |
| Visit 06 Category 3 (n=31) | 0 | | | |
| Visit 07 Category 1 (n=29) | 58.6 | | | |
| Visit 07 Category 2 (n=29) | 41.4 | | | |
| Visit 07 Category 3 (n=29) | 0 | | | |
| Visit 08 Category 1 (n=27) | 55.6 | | | |
| Visit 08 Category 2 (n=27) | 44.4 | | | |
| Visit 08 Category 3 (n=27) | 0 | | | |
| Visit 09 Category 1 (n=24) | 62.5 | | | |
| Visit 09 Category 2 (n=24) | 37.5 | | | |
| Visit 09 Category 3 (n=24) | 0 | | | |
| Visit 10 Category 1 (n=21) | 42.9 | | | |
| Visit 10 Category 2 (n=21) | 57.1 | | | |
| Visit 10 Category 3 (n=21) | 0 | | | |
| Visit 11 Category 1 (n=13) | 46.2 | | | |
| Visit 11 Category 2 (n=13) | 53.8 | | | |
| Visit 11 Category 3 (n=13) | 0 | | | |
| Visit 12 Category 1 (n=11) | 45.5 | | | |
| Visit 12 Category 2 (n=11) | 54.5 | | | |
| Visit 12 Category 3 (n=11) | 0 | | | |
| Visit 13 Category 1 (n=9) | 55.6 | | | |
| Visit 13 Category 2 (n=9) | 44.4 | | | |
| Visit 13 Category 3 (n=9) | 0 | | | |
| Visit 14 Category 1 (n=8) | 50 | | | |
| Visit 14 Category 2 (n=8) | 50 | | | |
| Visit 14 Category 3 (n=8) | 0 | | | |
| Visit 15 Category 1 (n=5) | 40 | | | |
| Visit 15 Category 2 (n=5) | 60 | | | |
| Visit 15 Category 3 (n=5) | 0 | | | |
| Visit 16 Category 1 (n=4) | 25 | | | |
| Visit 16 Category 2 (n=4) | 75 | | | |
| Visit 16 Category 3 (n=4) | 0 | | | |
| Visit 17 Category 1 (n=4) | 25 | | | |
| Visit 17 Category 2 (n=4) | 75 | | | |
| Visit 17 Category 3 (n=4) | 0 | | | |
| Visit 18 Category 1 (n=3) | 33.3 | | | |
| Visit 18 Category 2 (n=3) | 66.7 | | | |
| Visit 18 Category 3 (n=3) | 0 | | | |
| Visit 19 Category 1 (n=2) | 50 | | | |
| Visit 19 Category 2 (n=2) | 50 | | | |
| Visit 19 Category 3 (n=2) | 0 | | | |
| Visit 20 Category 1 (n=2) | 50 | | | |
| Visit 20 Category 2 (n=2) | 50 | | | |
| Visit 20 Category 3 (n=2) | 0 | | | |
| Visit 21 Category 1 (n=2) | 50 | | | |
| Visit 21 Category 2 (n=2) | 50 | | | |
| Visit 21 Category 3 (n=2) | 0 | | | |
| Visit 22 Category 1 (n=1) | 0 | | | |
| Visit 22 Category 2 (n=1) | 100 | | | |
| Visit 22 Category 3 (n=1) | 0 | | | |
| Visit 23 Category 1 (n=1) | 0 | | | |
| Visit 23 Category 2 (n=1) | 100 | | | |

| | | | | |
|----------------------------------------|------|--|--|--|
| Visit 23 Category 3 (n=1) | 0 | | | |
| Visit 24 Category 1 (n=1) | 0 | | | |
| Visit 24 Category 2 (n=1) | 100 | | | |
| Visit 24 Category 3 (n=1) | 0 | | | |
| Visit 25 Category 1 (n=1) | 0 | | | |
| Visit 25 Category 2 (n=1) | 100 | | | |
| Visit 25 Category 3 (n=1) | 0 | | | |
| Final visit/Withdraw Category 1 (n=21) | 33.3 | | | |
| Final visit/Withdraw Category 2 (n=21) | 66.7 | | | |
| Final visit/Withdraw Category 3 (n=21) | 0 | | | |

Notes:

[17] - n = number of participants analyzed at for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Problems With Self-Care as Assessed Using the EQ-5D

| | |
|-----------------|-------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Problems With Self-Care as Assessed Using the EQ-5D |
|-----------------|-------------------------------------------------------------------------------------|

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their self-care as the following categories: Category 1. I have no problems with self-care; Category 2. I have some problems washing or dressing myself; Category 3. I am unable to wash or dress myself. Analysis was performed on the ITT Population.

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

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
|-----------------------------------|-------------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 ^[18] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Screening Category 1 (n=41) | 78 | | | |
| Screening Category 2 (n=41) | 17.1 | | | |
| Screening Category 3 (n=41) | 4.9 | | | |
| Visit 01 Category 1 (n=20) | 80 | | | |
| Visit 01 Category 2 (n=20) | 20 | | | |
| Visit 01 Category 3 (n=20) | 0 | | | |
| Visit 02 Category 1 (n=33) | 81.8 | | | |
| Visit 02 Category 2 (n=33) | 18.2 | | | |
| Visit 02 Category 3 (n=33) | 0 | | | |
| Visit 03 Category 1 (n=29) | 86.2 | | | |
| Visit 03 Category 2 (n=29) | 13.8 | | | |
| Visit 03 Category 3 (n=29) | 0 | | | |

| | | | | |
|----------------------------|------|--|--|--|
| Visit 04 Category 1 (n=28) | 82.1 | | | |
| Visit 04 Category 2 (n=28) | 17.9 | | | |
| Visit 04 Category 3 (n=28) | 0 | | | |
| Visit 05 Category 1 (n=33) | 78.8 | | | |
| Visit 05 Category 2 (n=33) | 21.2 | | | |
| Visit 05 Category 3 (n=33) | 0 | | | |
| Visit 06 Category 1 (n=31) | 83.9 | | | |
| Visit 06 Category 2 (n=31) | 16.1 | | | |
| Visit 06 Category 3 (n=31) | 0 | | | |
| Visit 07 Category 1 (n=29) | 79.3 | | | |
| Visit 07 Category 2 (n=29) | 20.7 | | | |
| Visit 07 Category 3 (n=29) | 0 | | | |
| Visit 08 Category 1 (n=27) | 85.2 | | | |
| Visit 08 Category 2 (n=27) | 14.8 | | | |
| Visit 08 Category 3 (n=27) | 0 | | | |
| Visit 09 Category 1 (n=24) | 75 | | | |
| Visit 09 Category 2 (n=24) | 25 | | | |
| Visit 09 Category 3 (n=24) | 0 | | | |
| Visit 10 Category 1 (n=21) | 71.4 | | | |
| Visit 10 Category 2 (n=21) | 28.6 | | | |
| Visit 10 Category 3 (n=21) | 0 | | | |
| Visit 11 Category 1 (n=13) | 61.5 | | | |
| Visit 11 Category 2 (n=13) | 38.5 | | | |
| Visit 11 Category 3 (n=13) | 0 | | | |
| Visit 12 Category 1 (n=11) | 54.5 | | | |
| Visit 12 Category 2 (n=11) | 45.5 | | | |
| Visit 12 Category 3 (n=11) | 0 | | | |
| Visit 13 Category 1 (n=9) | 55.6 | | | |
| Visit 13 Category 2 (n=9) | 44.4 | | | |
| Visit 13 Category 3 (n=9) | 0 | | | |
| Visit 14 Category 1 (n=8) | 62.5 | | | |
| Visit 14 Category 2 (n=8) | 37.5 | | | |
| Visit 14 Category 3 (n=8) | 0 | | | |
| Visit 15 Category 1 (n=5) | 40 | | | |
| Visit 15 Category 2 (n=5) | 60 | | | |
| Visit 15 Category 3 (n=5) | 0 | | | |
| Visit 16 Category 1 (n=4) | 50 | | | |
| Visit 16 Category 2 (n=4) | 50 | | | |
| Visit 16 Category 3 (n=4) | 0 | | | |
| Visit 17 Category 1 (n=4) | 50 | | | |
| Visit 17 Category 2 (n=4) | 50 | | | |
| Visit 17 Category 3 (n=4) | 0 | | | |
| Visit 18 Category 1 (n=3) | 33.3 | | | |
| Visit 18 Category 2 (n=3) | 66.7 | | | |
| Visit 18 Category 3 (n=3) | 0 | | | |
| Visit 19 Category 1 (n=2) | 50 | | | |
| Visit 19 Category 2 (n=2) | 50 | | | |
| Visit 19 Category 3 (n=2) | 0 | | | |
| Visit 20 Category 1 (n=2) | 50 | | | |
| Visit 20 Category 2 (n=2) | 50 | | | |
| Visit 20 Category 3 (n=2) | 0 | | | |
| Visit 21 Category 1 (n=2) | 50 | | | |

| | | | | |
|----------------------------------------|------|--|--|--|
| Visit 21 Category 2 (n=2) | 50 | | | |
| Visit 21 Category 3 (n=2) | 0 | | | |
| Visit 22 Category 1 (n=1) | 100 | | | |
| Visit 22 Category 2 (n=1) | 0 | | | |
| Visit 22 Category 3 (n=1) | 0 | | | |
| Visit 23 Category 1 (n=1) | 0 | | | |
| Visit 23 Category 2 (n=1) | 100 | | | |
| Visit 23 Category 3 (n=1) | 0 | | | |
| Visit 24 Category 1 (n=1) | 0 | | | |
| Visit 24 Category 2 (n=1) | 100 | | | |
| Visit 24 Category 3 (n=1) | 0 | | | |
| Visit 25 Category 1 (n=1) | 0 | | | |
| Visit 25 Category 2 (n=1) | 100 | | | |
| Visit 25 Category 3 (n=1) | 0 | | | |
| Final Visit/Withdraw Category 1 (n=21) | 66.7 | | | |
| Final Visit/Withdraw Category 2 (n=21) | 33.3 | | | |
| Final Visit/Withdraw Category 3 (n=21) | 0 | | | |

Notes:

[18] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Problems With Usual Activities as Assessed Using the EQ-5D

| | |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Problems With Usual Activities as Assessed Using the EQ-5D |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their ability to perform usual activities as the following categories: Category 1. I have no problems with performing my usual activities; Category 2. I have some problems with performing my usual activities; Category 3. I am unable to perform my usual activities. Analysis was performed on the ITT Population.

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

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

| | | | | |
|-----------------------------------|-------------------------------------------|--|--|--|
| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 ^[19] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Screening Category 1 (n=41) | 39 | | | |
| Screening Category 2 (n=41) | 46.3 | | | |
| Screening Category 3 (n=41) | 14.6 | | | |
| Visit 01 Category 1 (n=20) | 40 | | | |
| Visit 01 Category 2 (n=20) | 50 | | | |

| | | | | |
|----------------------------|------|--|--|--|
| Visit 01 Category 3 (n=20) | 10 | | | |
| Visit 02 Category 1 (n=33) | 36.4 | | | |
| Visit 02 Category 2 (n=33) | 60.6 | | | |
| Visit 02 Category 3 (n=33) | 3 | | | |
| Visit 03 Category 1 (n=30) | 40 | | | |
| Visit 03 Category 2 (n=30) | 53.3 | | | |
| Visit 03 Category 3 (n=30) | 6.7 | | | |
| Visit 04 Category 1 (n=29) | 51.7 | | | |
| Visit 04 Category 2 (n=29) | 44.8 | | | |
| Visit 04 Category 3 (n=29) | 3.4 | | | |
| Visit 05 Category 1 (n=33) | 51.5 | | | |
| Visit 05 Category 2 (n=33) | 48.5 | | | |
| Visit 05 Category 3 (n=33) | 0 | | | |
| Visit 06 Category 1 (n=31) | 45.2 | | | |
| Visit 06 Category 2 (n=31) | 54.8 | | | |
| Visit 06 Category 3 (n=31) | 0 | | | |
| Visit 07 Category 1 (n=29) | 48.3 | | | |
| Visit 07 Category 2 (n=29) | 51.7 | | | |
| Visit 07 Category 3 (n=29) | 0 | | | |
| Visit 08 Category 1 (n=27) | 40.7 | | | |
| Visit 08 Category 2 (n=27) | 59.3 | | | |
| Visit 08 Category 3 (n=27) | 0 | | | |
| Visit 09 Category 1 (n=24) | 33.3 | | | |
| Visit 09 Category 2 (n=24) | 66.7 | | | |
| Visit 09 Category 3 (n=24) | 0 | | | |
| Visit 10 Category 1 (n=21) | 38.1 | | | |
| Visit 10 Category 2 (n=21) | 61.9 | | | |
| Visit 10 Category 3 (n=21) | 0 | | | |
| Visit 11 Category 1 (n=13) | 30.8 | | | |
| Visit 11 Category 2 (n=13) | 69.2 | | | |
| Visit 11 Category 3 (n=13) | 0 | | | |
| Visit 12 Category 1 (n=11) | 27.3 | | | |
| Visit 12 Category 2 (n=11) | 72.7 | | | |
| Visit 12 Category 3 (n=11) | 0 | | | |
| Visit 13 Category 1 (n=9) | 22.2 | | | |
| Visit 13 Category 2 (n=9) | 77.8 | | | |
| Visit 13 Category 3 (n=9) | 0 | | | |
| Visit 14 Category 1 (n=8) | 37.5 | | | |
| Visit 14 Category 2 (n=8) | 62.5 | | | |
| Visit 14 Category 3 (n=8) | 0 | | | |
| Visit 15 Category 1 (n=5) | 20 | | | |
| Visit 15 Category 2 (n=5) | 80 | | | |
| Visit 15 Category 3 (n=5) | 0 | | | |
| Visit 16 Category 1 (n=4) | 25 | | | |
| Visit 16 Category 2 (n=4) | 75 | | | |
| Visit 16 Category 3 (n=4) | 0 | | | |
| Visit 17 Category 1 (n=4) | 25 | | | |
| Visit 17 Category 2 (n=4) | 75 | | | |
| Visit 17 Category 3 (n=4) | 0 | | | |
| Visit 18 Category 1 (n=3) | 33.3 | | | |
| Visit 18 Category 2 (n=3) | 66.7 | | | |
| Visit 18 Category 3 (n=3) | 0 | | | |

| | | | | |
|------------------------------------------|------|--|--|--|
| Visit 19 Category 1 (n=2) | 50 | | | |
| Visit 19 Category 2 (n=2) | 50 | | | |
| Visit 19 Category 3 (n=2) | 0 | | | |
| Visit 20 Category 1 (n=2) | 50 | | | |
| Visit 20 Category 2 (n=2) | 50 | | | |
| Visit 20 Category 3 (n=2) | 0 | | | |
| Visit 21 Category 1 (n=2) | 50 | | | |
| Visit 21 Category 2 (n=2) | 50 | | | |
| Visit 21 Category 3 (n=2) | 0 | | | |
| Visit 22 Category 1 (n=1) | 0 | | | |
| Visit 22 Category 2 (n=1) | 100 | | | |
| Visit 22 Category 3 (n=1) | 0 | | | |
| Visit 23 Category 1 (n=1) | 0 | | | |
| Visit 23 Category 2 (n=1) | 100 | | | |
| Visit 23 Category 3 (n=1) | 0 | | | |
| Visit 24 Category 1 (n=1) | 0 | | | |
| Visit 24 Category 2 (n=1) | 100 | | | |
| Visit 24 Category 3 (n=1) | 0 | | | |
| Visit 25 Category 1 (n=1) | 0 | | | |
| Visit 25 Category 2 (n=1) | 100 | | | |
| Visit 25 Category 3 (n=1) | 0 | | | |
| Final Visit/Withdrawal Category 1 (n=21) | 33.3 | | | |
| Final Visit/Withdrawal Category 2 (n=21) | 61.9 | | | |
| Final Visit/Withdrawal Category 3 (n=21) | 4.8 | | | |

Notes:

[19] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Pain/Discomfort as Assessed Using the EQ-5D

| | |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Percentage of Participants With Pain/Discomfort as Assessed Using the EQ-5D |
|-----------------|-----------------------------------------------------------------------------|

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their pain as the following categories: Category 1. I have no pain or discomfort; Category 2. I have moderate pain or discomfort; Category 3. I have extreme pain or discomfort. Analysis was performed on the ITT Population.

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

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

| | | | | |
|-----------------------------------|-------------------------------------------|--|--|--|
| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 ^[20] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Screening Category 1 (n=41) | 29.3 | | | |
| Screening Category 2 (n=41) | 63.4 | | | |
| Screening Category 3 (n=41) | 7.3 | | | |
| Visit 01 Category 1 (n=20) | 10 | | | |
| Visit 01 Category 2 (n=20) | 85 | | | |
| Visit 01 Category 3 (n=20) | 5 | | | |
| Visit 02 Category 1 (n=32) | 43.8 | | | |
| Visit 02 Category 2 (n=32) | 56.3 | | | |
| Visit 02 Category 3 (n=32) | 0 | | | |
| Visit 03 Category 1 (n=30) | 40 | | | |
| Visit 03 Category 2 (n=30) | 60 | | | |
| Visit 03 Category 3 (n=30) | 0 | | | |
| Visit 04 Category 1 (n=29) | 55.2 | | | |
| Visit 04 Category 2 (n=29) | 37.9 | | | |
| Visit 04 Category 3 (n=29) | 6.9 | | | |
| Visit 05 Category 1 (n=33) | 45.5 | | | |
| Visit 05 Category 2 (n=33) | 51.5 | | | |
| Visit 05 Category 3 (n=33) | 3 | | | |
| Visit 06 Category 1 (n=31) | 48.4 | | | |
| Visit 06 Category 2 (n=31) | 51.6 | | | |
| Visit 06 Category 3 (n=31) | 0 | | | |
| Visit 07 Category 1 (n=29) | 48.3 | | | |
| Visit 07 Category 2 (n=29) | 51.7 | | | |
| Visit 07 Category 3 (n=29) | 0 | | | |
| Visit 08 Category 1 (n=27) | 37 | | | |
| Visit 08 Category 2 (n=27) | 59.3 | | | |
| Visit 08 Category 3 (n=27) | 3.7 | | | |
| Visit 09 Category 1 (n=24) | 50 | | | |
| Visit 09 Category 2 (n=24) | 37.5 | | | |
| Visit 09 Category 3 (n=24) | 12.5 | | | |
| Visit 10 Category 1 (n=21) | 42.9 | | | |
| Visit 10 Category 2 (n=21) | 47.6 | | | |
| Visit 10 Category 3 (n=21) | 9.5 | | | |
| Visit 11 Category 1 (n=13) | 46.2 | | | |
| Visit 11 Category 2 (n=13) | 53.8 | | | |
| Visit 11 Category 3 (n=13) | 0 | | | |
| Visit 12 Category 1 (n=11) | 45.5 | | | |
| Visit 12 Category 2 (n=11) | 36.4 | | | |
| Visit 12 Category 3 (n=11) | 18.2 | | | |
| Visit 13 Category 1 (n=9) | 44.4 | | | |
| Visit 13 Category 2 (n=9) | 55.6 | | | |
| Visit 13 Category 3 (n=9) | 0 | | | |
| Visit 14 Category 1 (n=8) | 62.5 | | | |
| Visit 14 Category 2 (n=8) | 37.5 | | | |
| Visit 14 Category 3 (n=8) | 0 | | | |

| | | | | |
|------------------------------------------|------|--|--|--|
| Visit 15 Category 1 (n=5) | 60 | | | |
| Visit 15 Category 2 (n=5) | 40 | | | |
| Visit 15 Category 3 (n=5) | 0 | | | |
| Visit 16 Category 1 (n=4) | 25 | | | |
| Visit 16 Category 2 (n=4) | 75 | | | |
| Visit 16 Category 3 (n=4) | 0 | | | |
| Visit 17 Category 1 (n=4) | 25 | | | |
| Visit 17 Category 2 (n=4) | 75 | | | |
| Visit 17 Category 3 (n=4) | 0 | | | |
| Visit 18 Category 1 (n=3) | 0 | | | |
| Visit 18 Category 2 (n=3) | 100 | | | |
| Visit 18 Category 3 (n=3) | 0 | | | |
| Visit 19 Category 1 (n=2) | 0 | | | |
| Visit 19 Category 2 (n=2) | 100 | | | |
| Visit 19 Category 3 (n=2) | 0 | | | |
| Visit 20 Category 1 (n=2) | 0 | | | |
| Visit 20 Category 2 (n=2) | 100 | | | |
| Visit 20 Category 3 (n=2) | 0 | | | |
| Visit 21 Category 1 (n=2) | 0 | | | |
| Visit 21 Category 2 (n=2) | 100 | | | |
| Visit 21 Category 3 (n=2) | 0 | | | |
| Visit 22 Category 1 (n=1) | 100 | | | |
| Visit 22 Category 2 (n=1) | 0 | | | |
| Visit 22 Category 3 (n=1) | 0 | | | |
| Visit 23 Category 1 (n=1) | 0 | | | |
| Visit 23 Category 2 (n=1) | 100 | | | |
| Visit 23 Category 3 (n=1) | 0 | | | |
| Visit 24 Category 1 (n=1) | 0 | | | |
| Visit 24 Category 2 (n=1) | 100 | | | |
| Visit 24 Category 3 (n=1) | 0 | | | |
| Visit 25 Category 1 (n=1) | 0 | | | |
| Visit 25 Category 2 (n=1) | 100 | | | |
| Visit 25 Category 3 (n=1) | 0 | | | |
| Final Visit/Withdrawal Category 1 (n=21) | 38.1 | | | |
| Final Visit/Withdrawal Category 2 (n=21) | 57.1 | | | |
| Final Visit/Withdrawal Category 3 (n=21) | 4.8 | | | |

Notes:

[20] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anxiety/Depression as Assessed Using the EQ-5D

| | |
|-----------------|--------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Anxiety/Depression as Assessed Using the EQ-5D |
|-----------------|--------------------------------------------------------------------------------|

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their pain as

the following categories: Category 1. I am not anxious or depressed; Category 2. I am moderately anxious or depressed; Category 3. I am extremely anxious or depressed. Analysis was performed on the ITT Population.

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

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

| End point values | Erlotinib 150 milligrams per day (mg/day) | | | |
|-----------------------------------|-------------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 ^[21] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Screening Category 1 (n=40) | 52.5 | | | |
| Screening Category 2 (n=40) | 37.5 | | | |
| Screening Category 3 (n=40) | 10 | | | |
| Visit 01 Category 1 (n=19) | 57.9 | | | |
| Visit 01 Category 2 (n=19) | 42.1 | | | |
| Visit 01 Category 3 (n=19) | 0 | | | |
| Visit 02 Category 1 (n=33) | 57.6 | | | |
| Visit 02 Category 2 (n=33) | 42.4 | | | |
| Visit 02 Category 3 (n=33) | 0 | | | |
| Visit 03 Category 1 (n=30) | 43.3 | | | |
| Visit 03 Category 2 (n=30) | 56.7 | | | |
| Visit 03 Category 3 (n=30) | 0 | | | |
| Visit 04 Category 1 (n=29) | 58.6 | | | |
| Visit 04 Category 2 (n=29) | 41.4 | | | |
| Visit 04 Category 3 (n=29) | 0 | | | |
| Visit 05 Category 1 (n=33) | 60.6 | | | |
| Visit 05 Category 2 (n=33) | 36.4 | | | |
| Visit 05 Category 3 (n=33) | 3 | | | |
| Visit 06 Category 1 (n=31) | 48.4 | | | |
| Visit 06 Category 2 (n=31) | 51.6 | | | |
| Visit 06 Category 3 (n=31) | 0 | | | |
| Visit 07 Category 1 (n=29) | 62.1 | | | |
| Visit 07 Category 2 (n=29) | 37.9 | | | |
| Visit 07 Category 3 (n=29) | 0 | | | |
| Visit 08 Category 1 (n=27) | 55.6 | | | |
| Visit 08 Category 2 (n=27) | 44.4 | | | |
| Visit 08 Category 3 (n=27) | 0 | | | |
| Visit 09 Category 1 (n=24) | 62.5 | | | |
| Visit 09 Category 2 (n=24) | 25 | | | |
| Visit 09 Category 3 (n=24) | 12.5 | | | |
| Visit 10 Category 1 (n=21) | 61.9 | | | |
| Visit 10 Category 2 (n=21) | 28.6 | | | |
| Visit 10 Category 3 (n=21) | 9.5 | | | |
| Visit 11 Category 1 (n=13) | 61.5 | | | |
| Visit 11 Category 2 (n=13) | 30.8 | | | |

| | | | | |
|---------------------------------------------|------|--|--|--|
| Visit 11 Category 3 (n=13) | 7.7 | | | |
| Visit 12 Category 1 (n=11) | 45.5 | | | |
| Visit 12 Category 2 (n=11) | 45.5 | | | |
| Visit 12 Category 3 (n=11) | 9.1 | | | |
| Visit 13 Category 1 (n=9) | 77.8 | | | |
| Visit 13 Category 2 (n=9) | 22.2 | | | |
| Visit 13 Category 3 (n=9) | 0 | | | |
| Visit 14 Category 1 (n=8) | 75 | | | |
| Visit 14 Category 2 (n=8) | 25 | | | |
| Visit 14 Category 3 (n=8) | 0 | | | |
| Visit 15 Category 1 (n=5) | 60 | | | |
| Visit 15 Category 2 (n=5) | 40 | | | |
| Visit 15 Category 3 (n=5) | 0 | | | |
| Visit 16 Category 1 (n=4) | 75 | | | |
| Visit 16 Category 2 (n=4) | 25 | | | |
| Visit 16 Category 3 (n=4) | 0 | | | |
| Visit 17 Category 1 (n=4) | 75 | | | |
| Visit 17 Category 2 (n=4) | 25 | | | |
| Visit 17 Category 3 (n=4) | 0 | | | |
| Visit 18 Category 1 (n=3) | 66.7 | | | |
| Visit 18 Category 2 (n=3) | 33.3 | | | |
| Visit 18 Category 3 (n=3) | 0 | | | |
| Visit 19 Category 1 (n=2) | 50 | | | |
| Visit 19 Category 2 (n=2) | 50 | | | |
| Visit 19 Category 3 (n=2) | 0 | | | |
| Visit 20 Category 1 (n=2) | 50 | | | |
| Visit 20 Category 2 (n=2) | 50 | | | |
| Visit 20 Category 3 (n=2) | 0 | | | |
| Visit 21 Category 1 (n=2) | 50 | | | |
| Visit 21 Category 2 (n=2) | 50 | | | |
| Visit 21 Category 3 (n=2) | 0 | | | |
| Visit 22 Category 1 (n=1) | 100 | | | |
| Visit 22 Category 2 (n=1) | 0 | | | |
| Visit 22 Category 3 (n=1) | 0 | | | |
| Visit 23 Category 1 (n=1) | 0 | | | |
| Visit 23 Category 2 (n=1) | 100 | | | |
| Visit 23 Category 3 (n=1) | 0 | | | |
| Visit 24 Category 1 (n=1) | 0 | | | |
| Visit 24 Category 2 (n=1) | 100 | | | |
| Visit 24 Category 3 (n=1) | 0 | | | |
| Visit 25 Category 1 (n=1) | 0 | | | |
| Visit 25 Category 2 (n=1) | 100 | | | |
| Visit 25 Category 3 (n=1) | 0 | | | |
| Final Visit/Withdrawal Category 1 (n=21) | 57.1 | | | |
| Final Visit/Withdrawal Category 2 (n=21) | 38.1 | | | |
| Final Visit/Withdrawal Category 3 (n=21) | 4.8 | | | |

Notes:

[21] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from Visit 1 (Baseline) until 30 days after the Final/Withdrawal Visit.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Erlotinib |
|-----------------------|-----------|

Reporting group description:

During the Treatment Phase participants found to have a tumour with EGFR exon 19 deletion or exon 21 (L858R) mutations received erlotinib 150 mg/day as a single oral dose until PD, death, unacceptable toxicity or withdrawal of consent.

| Serious adverse events | Erlotinib | | |
|---------------------------------------------------|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 41 (39.02%) | | |
| number of deaths (all causes) | 9 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |

| | | | |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Presyncope | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences causally related to treatment / all | 3 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Respiratory failure | | | |

| | | | |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|-------------------------------------------------------|------------------|--|--|
| Non-serious adverse events | Erlotinib | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 41 (97.56%) | | |
| Investigations | | | |
| Pulmonary function test decreased | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | | |
| occurrences (all) | 8 | | |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 41 (17.07%) | | |
| occurrences (all) | 9 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Chest pain | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Fatigue | | | |
| subjects affected / exposed | 14 / 41 (34.15%) | | |
| occurrences (all) | 17 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | | |
| occurrences (all) | 6 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 7 / 41 (17.07%) | | |
| occurrences (all) | 10 | | |
| Pain | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 4 | | |
| Dry eye | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Vision blurred | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences (all) | 5 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Constipation | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 10 | | |
| Diarrhoea | | | |

| | | | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspepsia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oral pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>26 / 41 (63.41%)</p> <p>40</p> <p>3 / 41 (7.32%)</p> <p>3</p> <p>11 / 41 (26.83%)</p> <p>14</p> <p>5 / 41 (12.20%)</p> <p>5</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>10 / 41 (24.39%)</p> <p>11</p> <p>5 / 41 (12.20%)</p> <p>7</p> <p>5 / 41 (12.20%)</p> <p>5</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Alopecia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dermatitis acneiform</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dry skin</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Palmar-plantar erythrodysaesthesia syndrome</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> | <p>9 / 41 (21.95%)</p> <p>9</p> <p>5 / 41 (12.20%)</p> <p>5</p> <p>13 / 41 (31.71%)</p> <p>15</p> <p>3 / 41 (7.32%)</p> <p>8</p> | | |

| | | | |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Rash | | | |
| subjects affected / exposed | 26 / 41 (63.41%) | | |
| occurrences (all) | 42 | | |
| Skin ulcer | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 7 / 41 (17.07%) | | |
| occurrences (all) | 7 | | |
| Back pain | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | | |
| occurrences (all) | 8 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 5 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 5 | | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Paronychia | | | |

| | | | |
|------------------------------------|------------------|--|--|
| subjects affected / exposed | 8 / 41 (19.51%) | | |
| occurrences (all) | 9 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 10 / 41 (24.39%) | | |
| occurrences (all) | 10 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 04 April 2011 | This amendment clarified that participants with previous treatment with NSCLC with chemotherapy were not excluded if the chemotherapy was neo-adjuvant or adjuvant and was completed > 6 months prior to consent for the diagnostic phase of the study. Physical examination, vital signs and EQ-5D were added to the text on the 'final visit/withdrawal from study' assessments to make the text consistent with the table of assessments. Shelf life of erlotinib was updated to 4 years. RECIST criteria to be used was updated from version 1.0 to 1.1. |
| 28 November 2012 | A further approved indication for erlotinib was added. Introduction sections were updated to included additional publications. Administrative changes were documented. Number of participants to enter diagnostic phase was reduced from 1200 to 700. Number of participants to enter treatment phase was reduced from 120 to 60. It was specified that if the drug was to be destroyed it had to be done by a Roche approved vendor. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported