# Clinical trial results:
# A Phase II Multicentre Randomised, Parallel Group, Double-Blind, Placebo Controlled Study of ZD1839 (Iressa™) (250mg Tablet) Plus Best Supportive Care (BSC) Versus Placebo Plus BSC in Chemotherapy Naïve Patients with Advanced (Stage IIIB or IV) Non-Small Cell Lung Cancer
# (NSCLC) and Poor Performance Status INSTEP (Iressa NSCLC Trial Evaluating Poor Performance Patients)

## Summary

| | |
|---|---|
| EudraCT number | 2004-004206-25 |
| Trial protocol | IE CZ |
| Global end of trial date | 24 April 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 March 2017 |
| First version publication date | 15 March 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | D7913C00711 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00259064 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | One Medimmune Way, 101 ORD, 2233C, Gaithersburg, United States, MD 20878 |
| Public contact | Yuri Rukazenkov, AstraZeneca, +44 01625 231825, yuri.rukazenkov@astrazeneca.com |
| Scientific contact | Yuri Rukazenkov, AstraZeneca, +44 01625 231825, yuri.rukazenkov@astrazeneca.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 | 22 February 2007 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 February 2007 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 April 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To compare gefitinib (IRESSA™, ZD1839) + best supportive care (BSC) versus placebo + BSC in terms of progression-free survival (PFS).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 27 September 2004 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 26 |
| Country: Number of subjects enrolled | Canada: 114 |
| Country: Number of subjects enrolled | Czech Republic: 4 |
| Country: Number of subjects enrolled | Netherlands: 17 |
| Country: Number of subjects enrolled | United Kingdom: 40 |
| Worldwide total number of subjects | 201 |
| EEA total number of subjects | 61 |

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) | 36 |
| From 65 to 84 years | 147 |
| 85 years and over | 18 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Patients were screened prior to entry into study & were required to fulfil all inclusion/exclusion criteria which included: a diagnosis of NSCLC, locally advanced or metastatic disease, not amenable to curative surgery, radiotherapy or chemotherapy; Measurable disease according to RECIST; No prior chemotherapy, biological or immunological therapy.

### Period 1

| | |
|---|---|
| Period 1 title | Baseline |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

Blinding implementation details:

Patients were randomised in a ratio of 1:1 to receive either gefitinib 250 mg or matching placebo tablets in combination with BSC. Study treatment wasdispensed to patients in a double blind manner on Day 1 and every 12 weeks thereafter until the patient discontinued.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Gefitinib |

Arm description:

Gefitinib 250 mg plus Best Supportive Care

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

Dosage and administration details:

250 mg daily

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Matched Placebo plus Best Supportive Care

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

Dosage and administration details:

1 tablet daily

| Number of subjects in period 1 | Gefitinib | Placebo |
|---|---|---|
| Started | 100 | 101 |
| Completed | 100 | 101 |

| Period 2 | |
|---|---|
| Period 2 title | Overall Trial |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

Blinding implementation details:

Patients were randomised in a ratio of 1:1 to receive either gefitinib 250 mg or matching placebo tablets in combination with BSC. Study treatment wasdispensed to patients in a double blind manner on Day 1 and every 12 weeks thereafter until the patient discontinued.

| Arms | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Gefitinib |

Arm description:

Gefitinib 250 mg plus Best Supportive Care

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

Dosage and administration details:

250 mg daily

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Matched Placebo plus Best Supportive Care

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

Dosage and administration details:

1 tablet daily

| **Number of subjects in period 2** | Gefitinib | Placebo |
|---|---|---|
| Started | 100 | 101 |
| Completed | 99 | 99 |
| Not completed | 1 | 2 |
| Consent withdrawn by subject | 1 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Gefitinib |
| Reporting group description: Gefitinib 250 mg plus Best Supportive Care | |
| Reporting group title | Placebo |
| Reporting group description: Matched Placebo plus Best Supportive Care | |

| Reporting group values | Gefitinib | Placebo | Total |
|---|---|---|---|
| Number of subjects | 100 | 101 | 201 |
| Age Categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 19 | 17 | 36 |
| From 65-84 years | 73 | 74 | 147 |
| 85 years and over | 8 | 10 | 18 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 72.3 | 73.9 | |
| standard deviation | ± 9.5 | ± 9 | - |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 39 | 40 | 79 |
| Male | 61 | 61 | 122 |
| Race<br>Units: Subjects | | | |
| Caucasian | 96 | 97 | 193 |
| Oriental | 4 | 3 | 7 |
| other | 0 | 1 | 1 |
| Smoking history<br>Units: Subjects | | | |
| Habitual | 19 | 19 | 38 |
| Occasional | 0 | 2 | 2 |
| Ex Smoker | 71 | 71 | 142 |
| Non Smoker | 10 | 9 | 19 |
| WHO Performance Status | | | |
| World Health Organisation (WHO) performance status is a scale from 0 (fully active) to 5 (dead), indicating patients ability to perform certain activities of daily life. All patients in this study have PS of 2 or 3. | | | |
| Units: Subjects | | | |
| 2: in bed <= 50% of time | 55 | 63 | 118 |
| 3: in bed > 50% of time | 45 | 38 | 83 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Gefitinib |
| Reporting group description: Gefitinib 250 mg plus Best Supportive Care | |
| Reporting group title | Placebo |
| Reporting group description: Matched Placebo plus Best Supportive Care | |
| Reporting group title | Gefitinib |
| Reporting group description: Gefitinib 250 mg plus Best Supportive Care | |
| Reporting group title | Placebo |
| Reporting group description: Matched Placebo plus Best Supportive Care | |

### Primary: Progression Free Survival (PFS)

| | |
|---|---|
| End point title | Progression Free Survival (PFS) |
| End point description: Progression Free Survival (PFS) is defined as the interval between the date of randomisation and the earliest date of objective disease progression according to The Response Evaluation Criteria in Solid Tumours [RECIST] or death due to any cause in the absence of progression | |
| End point type | Primary |
| End point timeframe: Overall Study - Assessed every 6 weeks from randomisation | |

| End point values | Gefitinib | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 101 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 43 (39 to 55) | 41 (37 to 43) | | |

### Statistical analyses

| Statistical analysis title | Primary Analysis: Hazard Ratio |
|---|---|
| Statistical analysis description: Hazard Ratio(HR) calculated from Cox Proportional hazards model including factors (gender, WHO performance status, histology, smoking history, lung stage classification). The primary analysis does not include progression events, or deaths in the absence of progression, which occur more than 12 weeks after the last evaluable RECIST assessment. | |
| Comparison groups | Gefitinib v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 201 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | = 0.2165 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.821 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 1.123 |

Notes:

[1] - Although medians are presented these estimates of PFS are not reliable in this setting: scans were every 6 wks whilst the population progressed rapidly, over half the patients progressing before their first scan. Therefore medians will be more representative of scan timings, rather than actual progression times which may have occurred before the scan takes place. The HR is a much more accurate reflection of the treatment difference, taking into account all information over the study period.

## Secondary: Objective Response Rate

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

End point description:

Objective Response Rate is the number of patients who have either a complete response (CR) or partial reponse (PR) as defined by Response Evaluation Criteria In Solid Tumour (RECIST) during the study.

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

End point timeframe:

Overall Study - Response is assesed every 6 weeks from randomisation

| End point values | Gefitinib | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 101 | | |
| Units: Patients | 6 | 1 | | |

## Statistical analyses

| Statistical analysis title | Comparison of Objective Response Rate |
|---|---|

Statistical analysis description:

The objective tumour response rate was compared between gefitinib and placebo using a logistic regression model which included terms for Randomised Treatment, Gender, WHO Performance Status, Histology, Smoking History and Lung Stage Classification. The odds ratio (gefitinib:placebo) was estimated from the model along with its associated 95% CI.

| | |
|---|---|
| Comparison groups | Gefitinib v Placebo |
| Number of subjects included in analysis | 201 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 6.556 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.741 |
| upper limit | 58.173 |

## Secondary: Overall Survival (OS)

| | |
|---|---|
| End point title | Overall Survival (OS) |

End point description:

Overall survival (time to death) is defined as the interval between the date of randomisation and the date of patient death, due to any cause, or to the last date the patient was known to be alive. Those patients who are known to be alive at study closure will be regarded as censored in the calculation of the median overall survival time for each treatment group.

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

End point timeframe:

Assessed every 6 weeks from randomisation until study data cut off (DCO) or death

| **End point values** | Gefitinib | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 100 | 101 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 3.7 (2.6 to 4.4) | 2.8 (2.3 to 3.6) | | |

### Statistical analyses

| **Statistical analysis title** | Comparison of Overall Survival |
|---|---|

Statistical analysis description:

Overall survival (time to death) was analysed using a proportional hazards model. The model included terms for Randomised Treatment, Gender, WHO Performance Status, Histology, Smoking History and Lung Stage Classification. The hazard ratio (gefitinib:placebo) was estimated together with its associated 95% confidence interval and p-value.

| | |
|---|---|
| Comparison groups | Gefitinib v Placebo |
| Number of subjects included in analysis | 201 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2722 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.615 |
| upper limit | 1.147 |

## Secondary: Pulmonary symptom improvement

| End point title | Pulmonary symptom improvement |
|---|---|

End point description:

Pulmonary symptom improvement is calculated from the responses to the Pulmonary items on the Functional Assessment of Cancer Therapy (Lung) (FACT-L) questionnaire which are: shortness of breath; ease of breathing; tightness in chest and cough  A Pulmonary Symptom improvement is defined as an improvement from baseline in at least 1 moderate (score 1) or severe (score 0) pulmonary item of at least 2 points that is maintained for at least 28 days, ie, symptom improvement from moderate (score 1) to minimal (score 3) or none (score 4); or improvement from severe (score 0) to mild (score 2) or minimal (score 3) or none (score 4).

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

End point timeframe:

Collected three-weekly via a patient diary for all patients for the 1st 18 weeks, then every 6 weeks at each clinic visit up to and including 6 weeks post disease progression.

| **End point values** | Gefitinib | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 53[2] | 46[3] | | |
| Units: Patients | | | | |
| number (not applicable) | 15 | 13 | | |

Notes:

[2] - Patients analysed are those in the Evaluable-for-pulmonary-symptom-improvement population.

[3] - Patients analysed are those in the Evaluable-for-pulmonary-symptom-improvement population.

### Statistical analyses

| **Statistical analysis title** | Comparison of pulmonary sysmptom improvement |
|---|---|

Statistical analysis description:

The pulmonary symptom improvement rate was compared between gefitinib and placebousing a logistic regression model including terms for Randomised Treatment, Gender, WHO Performance Status, Histology, Smoking History and Lung Stage Classification. The odds ratio (gefitinib:placebo) will be estimated from the model along with its associated 95% CI.

| Comparison groups | Gefitinib v Placebo |
|---|---|
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[4] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.986 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.395 |
| upper limit | 2.46 |

Notes:

[4] - Patients analysed are those in the Evaluable-for-pulmonary-symptom-improvement population which included all patients who had at least one LCS pulmonaryitem (shortness of breath, ease of breathing, tightness in chest, or cough) with a baseline score of 0 or 1 (scores ranged from 0 to 4, with a higher score indicating better pulmonary symptoms) and who also had at least 1 evaluable post

baseline assessment.

## Secondary: Improvement in Quality of Life as measured by the Trial Outcome Index (TOI)

| End point title | Improvement in Quality of Life as measured by the Trial Outcome Index (TOI) |
|---|---|

End point description:

Improvement in patient-reported functionality as measured by TOI (trial outcome index), which is comprised of thephysical and functional well being sectionsand LCS of FACT-L. An improvemetnt is defined to be an increase from baseline score of 6 or more points.

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

End point timeframe:

Collected three-weekly via a patient diary for all patients for the 1st 18 weeks, then every 6 weeks at each clinic visit up to and including 6 weeks post disease progression.

| **End point values** | Gefitinib | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 76[5] | 65[6] | | |
| Units: patients | 12 | 9 | | |

Notes:

[5] - Patients analysed are those in the Evaluable for Quality of Life population, a subset of the ITT.

[6] - Patients analysed are those in the Evaluable for Quality of Life population, a subset of the ITT.

### Statistical analyses

| **Statistical analysis title** | Comparison of QoL improvement measured by the TOI |
|---|---|

Statistical analysis description:

The QoL (Quality of Life) improvement rate as measured by TOI (Trial outcome Index) was compared between gefitinib and placebo using a logistic regression model that includes terms for Randomised Treatment, Gender,WHO Performance Status, Histology, Smoking History and Lung Stage Classification. The odds ratio(gefitinib:placebo) was estimated from the model along with its associated 95% CI.

| Comparison groups | Gefitinib v Placebo |
|---|---|
| Number of subjects included in analysis | 141 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[7] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.033 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.381 |
| upper limit | 2.8 |

Notes:

[7] - Patients analysed are those in the Evaluable for Quality of Life population, including those with a baseline Quality of Life (QoL) assessment and at least one non-missing post-baseline QoL assessment. A subset of the ITT.

## Secondary: Improvement in Quality of Life as measured by the total score of the FACT-L questionnaire

| End point title | Improvement in Quality of Life as measured by the total score |
|---|---|

| | |
|---|---|
| | of the FACT-L questionnaire |

End point description:

Improvement in patient-reported functionality as measured by the total score of the FACT-L. An improvement is defined to be an increase from baseline score of 6 or more points.

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

End point timeframe:

Collected three-weekly via a patient diary for all patients for the 1st 18 weeks, then every 6 weeks at each clinic visit up to and including 6 weeks post disease progression.

| **End point values** | Gefitinib | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 76[8] | 65[9] | | |
| Units: patients | 16 | 13 | | |

Notes:

[8] - Patients analysed are those in the Evaluable for Quality of Life population, a subset of the ITT.

[9] - Patients analysed are those in the Evaluable for Quality of Life population, a subset of the ITT.

### Statistical analyses

| **Statistical analysis title** | Comparison of QoL improvement measured by FACT-L |
|---|---|

Statistical analysis description:

The QoL(Quality of Life) improvement rate measured by the total score of the FACT-L will be compared between gefitinib and placebo using a logistic regression model that includes terms for Randomised Treatment, Gender,WHO Performance Status, Histology, Smoking History and Lung Stage Classification. The odds ratio(gefitinib:placebo) will be estimated from the model along with its associated 95% CI.

| | |
|---|---|
| Comparison groups | Gefitinib v Placebo |
| Number of subjects included in analysis | 141 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[10] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.007 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.421 |
| upper limit | 2.408 |

Notes:

[10] - Patients analysed are those in the Evaluable for Quality of Life population, including those with a baseline Quality of Life (QoL) assessment and at least one non-missing post-baseline QoL assessment. A subset of the ITT.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs are collected every 21 days for 1st 18 wks, then every 42 days until discontinuation of study drug. At discontinuation, patients are followed up for all existing & new AEs for 30 days; all AEs, toxicities & SAEs should be followed until resolution.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 10.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Matched Placebo plus Best Supportive Care

| | |
|---|---|
| Reporting group title | Gefitinib |

Reporting group description:

Gefitinib 250 mg plus Best Supportive Care

| Serious adverse events | Placebo | Gefitinib | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 25 / 101 (24.75%) | 25 / 100 (25.00%) | |
| number of deaths (all causes) | 85 | 84 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| 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 | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Fatigue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung consolidation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Impaired self-care | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Rib fracture | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Ventricular tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Brain stem infarction | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cerebral disorder | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Convulsion | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Somnolence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (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 | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 2 / 100 (2.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Melaena | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 101 (1.98%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (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 | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess intestinal | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Corneal abscess | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected skin ulcer | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis viral | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mycobacterium avium complex | | | |

| | | | |
|---|---|---|---|
| infection | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 101 (2.97%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 0 / 100 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 100 (1.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Placebo | Gefitinib | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 92 / 101 (91.09%) | 89 / 100 (89.00%) | |
| Investigations | | | |
| Weight decrease | | | |
| subjects affected / exposed | 3 / 101 (2.97%) | 6 / 100 (6.00%) | |
| occurrences (all) | 3 | 6 | |

| | | | |
|---|---|---|---|
| Nervous system disorders | | | |
| Dizzines | | | |
| subjects affected / exposed | 7 / 101 (6.93%) | 4 / 100 (4.00%) | |
| occurrences (all) | 8 | 4 | |
| Headache | | | |
| subjects affected / exposed | 4 / 101 (3.96%) | 5 / 100 (5.00%) | |
| occurrences (all) | 6 | 7 | |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 5 / 100 (5.00%) | |
| occurrences (all) | 1 | 5 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 6 / 100 (6.00%) | |
| occurrences (all) | 1 | 6 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 7 / 101 (6.93%) | 9 / 100 (9.00%) | |
| occurrences (all) | 7 | 10 | |
| Fatigue | | | |
| subjects affected / exposed | 22 / 101 (21.78%) | 14 / 100 (14.00%) | |
| occurrences (all) | 22 | 14 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 13 / 101 (12.87%) | 13 / 100 (13.00%) | |
| occurrences (all) | 14 | 17 | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 101 (3.96%) | 6 / 100 (6.00%) | |
| occurrences (all) | 4 | 6 | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 101 (0.00%) | 5 / 100 (5.00%) | |
| occurrences (all) | 0 | 5 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 9 / 101 (8.91%) | 11 / 100 (11.00%) | |
| occurrences (all) | 9 | 11 | |
| Constipation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 19 / 101 (18.81%) | 17 / 100 (17.00%) | |
| occurrences (all) | 22 | 19 | |
| Diarrhoea | | | |
| subjects affected / exposed | 20 / 101 (19.80%) | 50 / 100 (50.00%) | |
| occurrences (all) | 24 | 65 | |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 101 (2.97%) | 6 / 100 (6.00%) | |
| occurrences (all) | 3 | 6 | |
| Dysphagia | | | |
| subjects affected / exposed | 4 / 101 (3.96%) | 5 / 100 (5.00%) | |
| occurrences (all) | 4 | 5 | |
| Nausea | | | |
| subjects affected / exposed | 31 / 101 (30.69%) | 30 / 100 (30.00%) | |
| occurrences (all) | 35 | 37 | |
| Stomatitis | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 9 / 100 (9.00%) | |
| occurrences (all) | 5 | 9 | |
| Vomiting | | | |
| subjects affected / exposed | 14 / 101 (13.86%) | 21 / 100 (21.00%) | |
| occurrences (all) | 15 | 24 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 11 / 101 (10.89%) | 6 / 100 (6.00%) | |
| occurrences (all) | 13 | 6 | |
| Dyspnoea | | | |
| subjects affected / exposed | 13 / 101 (12.87%) | 17 / 100 (17.00%) | |
| occurrences (all) | 13 | 17 | |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 101 (1.98%) | 6 / 100 (6.00%) | |
| occurrences (all) | 2 | 9 | |
| Haemoptysis | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 4 / 100 (4.00%) | |
| occurrences (all) | 5 | 5 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| Decubitis ulcer | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 5 / 100 (5.00%) | |
| occurrences (all) | 1 | 5 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 2 / 101 (1.98%) | 6 / 100 (6.00%) | |
| occurrences (all) | 2 | 6 | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 101 (0.99%) | 19 / 100 (19.00%) | |
| occurrences (all) | 1 | 23 | |
| Pruritis | | | |
| subjects affected / exposed | 2 / 101 (1.98%) | 9 / 100 (9.00%) | |
| occurrences (all) | 3 | 11 | |
| Rash | | | |
| subjects affected / exposed | 10 / 101 (9.90%) | 34 / 100 (34.00%) | |
| occurrences (all) | 14 | 41 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 9 / 100 (9.00%) | |
| occurrences (all) | 5 | 9 | |
| Confusional state | | | |
| subjects affected / exposed | 9 / 101 (8.91%) | 6 / 100 (6.00%) | |
| occurrences (all) | 9 | 6 | |
| Depression | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 2 / 100 (2.00%) | |
| occurrences (all) | 6 | 2 | |
| Insomnia | | | |
| subjects affected / exposed | 4 / 101 (3.96%) | 11 / 100 (11.00%) | |
| occurrences (all) | 4 | 12 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 8 / 101 (7.92%) | 7 / 100 (7.00%) | |
| occurrences (all) | 9 | 7 | |
| Muscular weakness | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 7 / 100 (7.00%) | |
| occurrences (all) | 5 | 7 | |
| Musculoskeletal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 101 (4.95%) | 7 / 100 (7.00%) | |
| occurrences (all) | 5 | 7 | |
| pain in extremity | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 4 / 100 (4.00%) | |
| occurrences (all) | 8 | 4 | |
| Infections and infestations | | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 7 / 101 (6.93%) | 11 / 100 (11.00%) | |
| occurrences (all) | 7 | 13 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 3 / 100 (3.00%) | |
| occurrences (all) | 5 | 3 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 101 (7.92%) | 8 / 100 (8.00%) | |
| occurrences (all) | 8 | 8 | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 17 / 101 (16.83%) | 20 / 100 (20.00%) | |
| occurrences (all) | 19 | 21 | |
| Dehydration | | | |
| subjects affected / exposed | 5 / 101 (4.95%) | 5 / 100 (5.00%) | |
| occurrences (all) | 5 | 6 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 17 October 2005 | Amendment included: Extension of recruitment period due to slow recruitment from 11 months to 27 months; Clarification of exploratory objectives, planned biomarker analyses and confirmation of the biomarkers to be investigated; Change to allow patients to continue receiving study medication following disease progression, if the patient is deriving clinical benefit; Updated information regarding ZD1839 exposure, including ISEL clinical study data and rodent carcinogenicity data; Clarification of timings for visit 1 and visit 2; Clarification of Exclusion Criteria, Item 2 (radiotherapy, to allow discrimination between wide field and local irradiation.); Confirmation that proteomics no longer applicable to this protocol; Clarification of the reporting requirements for overdose; confirmation that no germline genetic analysis will be performed on any tumour tissue from this study; correction of volume of blood sampling to be taken at baseline. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported