EU Clinical Trials Register

Clinical trial results:

A phase II Open Label, Multicentre, Single Arm Study to Characterise the Efficacy, Safety and Tolerability of Gefitinib 250 mg (IRESSA™) as treatment re-challenge in Patients, who have Epidermal Growth Factor Receptor (EGFR) Mutation Positive Locally Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) and who previously responded to gefitinib and received subsequent chemotherapy or other active anti-cancer therapy excluding EGFR-TKIs

Summary

EudraCT number	2011-005157-31
Trial protocol	IT
Global end of trial date	09 January 2015

Results information

Result version number	v1 (current)
This version publication date	23 June 2016
First version publication date	23 June 2016

Trial information

Trial identification

Sponsor protocol code	D7913L00138

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca SpA
Sponsor organisation address	Via Sforza 5, Milan, Italy, 20080
Public contact	Elisa Pastore, AstraZeneca SpA, +39 0298011,
Scientific contact	Silvia Ferrari, AstraZeneca SpA, +39 0298015227, silvia.ferrari@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	09 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 January 2015
Global end of trial reached?	Yes
Global end of trial date	09 January 2015
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 describe Objective response rate (ORR; confirmed complete response (CR) or partial response (PR) as per the Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 and the disease control rate (CBR; confirmed complete response (CR) or partial response (PR) or stable disease (SD)) of gefitinib using Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 in patients diagnosed for activating sensitising Epidermal Growth Factor mutation positive (EGFR M+) NSCLC.

Protection of trial subjects:

The Informed Consent Forms was incorporated wording that complies with relevant data protection and privacy legislation. Pursuant to this wording, patients authorised the collection, use and disclosure of their study data by the investigator and by those persons who need that information for the purposes of the study. The Master Informed Consent Forms explained that study data were stored in a computer database, maintaining confidentiality in accordance with national data legislation. All data computer processed by AstraZeneca were identified by "E-code", and study code. AstraZeneca did not provide individual genotype results to patients, any insurance company, any employer, their family members, general physician or any other third party, unless required to do so by the law. Extra precautions were taken to preserve confidentiality and prevent study data being linked to the identity of the patient. In exceptional circumstances, however, certain individuals might see both the study data and the personal identifiers of a patient. For example, in the case of a medical emergency, an AstraZeneca Physician or an investigator might know a patient's identity and also have access to his or her study data. Also Regulatory authorities may require access to the relevant files.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 July 2012
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	Italy: 61
Worldwide total number of subjects	61
EEA total number of subjects	61

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	21
From 65 to 84 years	39
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Investigator had to obtain signed informed consent from the potential patient before any study specific procedures are performed. He/she determined patient eligibility and assigned potential patient with a unique identification number. He/she recorded enrolment date for patients who were eligible for the study in the eCRF at screening Visit.

Pre-assignment period milestones

Number of subjects started	61
Number of subjects completed	61

Period 1

Period 1 title	Baseline period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	Gefitinib

Arm description:

Gefitinib 250 mg in oral tablet form administered once daily.

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

Dosage and administration details:

Gefitinib 250 mg in oral tablet form will be administered once daily.

Number of subjects in period 1	Gefitinib
Started	61
Completed	61

Period 2

Period 2 title	Open label phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Arm title	Gefitinib

Arm description:

Gefitinib 250 mg in oral tablet form administered once daily.

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

Dosage and administration details:

Gefitinib 250 mg in oral tablet form will be administered once daily.

Number of subjects in period 2	Gefitinib
Started	61
Completed	10
Not completed	51
Progressive disease (47), Other reason (1)	48
Adverse event, non-fatal	3

Baseline characteristics

Reporting groups

Reporting group title	Gefitinib
Reporting group description:	
Gefitinib 250 mg in oral tablet form administered once daily.	

Reporting group values	Gefitinib	Total	
Number of subjects	61	61	
Age Categorical			
Patient's age calculated at screening visit			
Units: Subjects			
Adults (18-64 years)	21	21	
From 65-84 years	39	39	
85 years and over	1	1	
Age Continuous			
Patient's age calculated at screening visit			
Units: years			
arithmetic mean	66.9		
standard deviation	± 10.1	-	
Gender Categorical			
Units: Subjects			
Female	45	45	
Male	16	16	

Subject analysis sets

Subject analysis set title	Gefitinib
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All enrolled patients	

Reporting group values	Gefitinib		
Number of subjects	61		
Age Categorical			
Patient's age calculated at screening visit			
Units: Subjects			
Adults (18-64 years)	21		
From 65-84 years	39		
85 years and over	1		
Age Continuous			
Patient's age calculated at screening visit			
Units: years			
arithmetic mean	66.9		
standard deviation	± 10.1		
Gender Categorical			
Units: Subjects			
Female	45		

Male	16		

End points

End points reporting groups

Reporting group title	Gefitinib
Reporting group description:	
Gefitinib 250 mg in oral tablet form administered once daily.	
Reporting group title	Gefitinib
Reporting group description:	
Gefitinib 250 mg in oral tablet form administered once daily.	
Subject analysis set title	Gefitinib
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All enrolled patients	

Primary: Objective Response Rate

End point title	Objective Response Rate[1]
End point description:	
ORR is the sum of CR and PR	
End point type	Primary
End point timeframe:	
Overall Study	

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: 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.

End point values	Gefitinib	Gefitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	61[2]	61[3]		
Units: percentage				
number (confidence interval 95%)	4.9 (1.7 to 13.5)	4.9 (1.7 to 13.5)		

Notes:

[2] - 3 patients with a response

[3] - 3 patients with a response

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Benefit Rate

End point title	Clinical Benefit Rate[4]
End point description:	
CBR is the sum of CR, PR and SD	
End point type	Primary
End point timeframe:	
Overall Study	

Notes:

[4] - 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: Analysis of ORR and CBR was based on frequency analysis (n,%) and 95% CI. I tried to add this info the form "Statsitical analysis" but an additional error appear. The system required the results of a group comparison. The study was a single arm trial.

End point values	Gefitinib	Gefitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	61[5]	61[6]		
Units: percentage				
number (confidence interval 95%)	52.5 (40.2 to 64.5)	52.5 (40.2 to 64.5)		

Notes:

[5] - 32 patients with CBR

[6] - 32 patients with CBR

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

PFS was calculated as the time from the first dose of gefitinib study treatment until the date of (i) objective disease progression as defined by RECIST 1.1 or (ii) death from any cause in the absence of progression.

End point type	Secondary

End point timeframe:

Overall Study

End point values	Gefitinib			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: Days				
median (confidence interval 95%)	84 (74 to 94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

OS was calculated as the time from the first dose of gefitinib study treatment until the date of death from any cause. Any patient not known to have died at the time of data analysis was censored at the time of the last recorded date on which the patient was known to be alive.

End point type	Secondary

End point timeframe:

Overall Study

End point values	Gefitinib			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: Days				
median (confidence interval 95%)	311 (268 to 431)			

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment duration with gefitinib

End point title	Treatment duration with gefitinib

End point description:

Treatment duration will be calculated from the date of first trial therapy intake to the date of last trial therapy taken.

End point type	Secondary

End point timeframe:

Overall Study

End point values	Gefitinib	Gefitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	61	61		
Units: Days				
median (confidence interval 95%)	108 (92 to 169)	108 (92 to 169)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to worsening of disease related symptoms

End point title	Time to worsening of disease related symptoms

End point description:

Time to worsening of disease-related symptoms based on FACT-L LCS was defined as the interval from the date of enrollment to the first visit response of 'worsened' without a subsequent response of 'improved' or 'no change' within 21 days (or to the last assessment), death due to any cause, or early discontinuation from the study. Time to worsening was censored at the last non-missing assessment visit if the worsening was not observed.

End point type	Secondary

End point timeframe:

Overall Study

End point values	Gefitinib			
Subject group type	Subject analysis set			
Number of subjects analysed	61[7]			
Units: Days				
median (confidence interval 95%)	93 (71 to 109)			

Notes:

[7] - Max score on FACT-L is 136.Worsening is defined as a change from baseline in total score <= -6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are those with start date beyond or equal to the informed consent date.
Analysis includes adverse events with starting date until 30 days after the last study drug dose intake.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Gefitinib

Reporting group description:

Gefitinib 250 mg in oral tablet form administered once daily.

Serious adverse events	Gefitinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 58 (17.24%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cognitive disorders			

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
subjects affected / exposed	2 / 58 (3.45%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			

subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 58 (1.72%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Gefitinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 58 (72.41%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	8		
Chest pain			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Fatigue			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	6		
General physical health deterioration			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	5		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	4		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	12		
Gastrointestinal disorders			
Diarrhea NOS			
subjects affected / exposed	16 / 58 (27.59%)		
occurrences (all)	21		
Vomiting alone			
subjects affected / exposed	9 / 58 (15.52%)		
occurrences (all)	11		
Nausea			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	8		
Abdominal pain upper			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		
Cough			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	9 / 58 (15.52%)		
occurrences (all)	13		
Dry skin			

subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	5		
Pruritus			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	6		
Dermatitis acneiform			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
skin toxicity			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	5 / 58 (8.62%)		
occurrences (all)	6		
Bone pain			
subjects affected / exposed	4 / 58 (6.90%)		
occurrences (all)	4		
Infections and infestations			
Folliculitis			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	3		
Paronychia			
subjects affected / exposed	3 / 58 (5.17%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 58 (10.34%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2013	At the previous text on measurable disease defined as at least one lesion, preferentially not previously irradiated, that can be accurately measured at baseline as ≥ 10 mm in the longest diameter (except lymph nodes which must have short axis ≥ 15 mm) with spiral CT or MRI and which is suitable for accurate repeated measurements was added that in the presence of only 1 lesion previously irradiated, this can be accepted if a progression of disease has been documented compared with the previous assessment or if the physician considers the modifications of the lesion worthy of a new treatment. Exclusion criteria #9 was modified and steroids were admitted if the purpose of their use was antiedemigenous prophylaxis, in absence of neurological symptoms. Total sample was reduced from 92 pateints to 54 evaluable patients. Statistical methods for analysis were better specified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported