ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 09/30/2015

ClinicalTrials.gov ID: NCT01378962

Study Identification

Unique Protocol ID: ML25514

Brief Title: A Study of Tarceva (Erlotinib) in Patients With Locally Advanced or Metastatic Non-Small Cell Lung Cancer (TRIGGER)

Official Title: Phase II, Open-label Study of Erlotinib (Tarceva®) Treatment in Patients With Locally Advanced or Metastatic Non-small-cell Lung Cancer Who Present Activating Mutations in the Tyrosine Kinase Domain of the Epidermal Growth Factor Receptor (EGFR) - (TRIGGER)

Secondary IDs:

Study Status

Record Verification: September 2015

Overall Status: Completed

Study Start: March 2011

Primary Completion: June 2014 [Actual]

Study Completion: June 2014 [Actual]

Sponsor/Collaborators

Sponsor: Hoffmann-La Roche

Responsible Party: Sponsor

Collaborators:

Oversight

FDA Regulated?: Yes

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 10/16/2010 Board Name: Comitato Etico delle Aziende Sanitarie dell'Umbria (CEAS Umbria) Board Affiliation: Comitato Etico delle Aziende Sanitarie dell'Umbria (CEAS Umbria) Phone: 00390755170199 Email: segreteria@ceasumbria.it
Data Monitoring?:	
Oversight Authorities:	Italy: Ministry of Health

Study Description

Brief Summary:	This single-arm, open-label study will evaluate the efficacy and safety of Tarceva (erlotinib) in patients with locally advanced or metastatic non-small cell lung cancer. Patients will receive daily oral doses of 150 mg Tarceva. The anticipated time on study treatment is 12 months.
Detailed Description:	

Conditions

Conditions:	Non-Squamous Non-Small Cell Lung Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	50 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Single Arm	Drug: erlotinib [Tarceva] 150 mg orally once a day for 12 months

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Adult patients, >/=18 years of age
- Locally advanced or metastatic non-small cell lung cancer
- Measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST)
- Eastern Cooperative Oncology Group (ECOG) performance status 0-2
- Life expectancy over >/=12 weeks
- Adequate hematological, liver, or kidney function

Exclusion Criteria:

- Previous therapy against epidermal growth factor receptor for metastatic disease
- Treatment with investigational drug during the 3 weeks before enrollment
- History of neoplasm
- Patients with symptomatic cerebral metastases
- Unstable systemic disease

Contacts/Locations

Study Officials: Clinical Trials
Hoffmann-La Roche

Locations: Italy
Perugia, Umbria, Italy, 06156

Pisa, Toscana, Italy, 56124

Rozzano, Lombardia, Italy, 20089

Catania, Sicilia, Italy, 95122

Milano, Lombardia, Italy, 20141

Bologna, Emilia-Romagna, Italy, 40133

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Roma, Lazio, Italy, 00168

Napoli, Campania, Italy, 80131

References

Citations:

Links:

Study Results

Participant Flow

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 milligrams (mg) tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Overall Study

	Erlotinib 150 mg
Started	50
Completed	33
Not Completed	17

	Erlotinib 150 mg
Death	14
Lost to Follow-up	1
Unspecified	2

Baseline Characteristics

Analysis Population Description

Safety population included all participants enrolled in the study who received at least 1 dose of treatment and had at least 1 safety assessment.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Baseline Measures

	Erlotinib 150 mg
Number of Participants	50
Age, Continuous [units: years] Mean (Standard Deviation)	62.86 (11.42)
Gender, Male/Female [units: participants]	
Female	34
Male	16

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression or Death at 12 Months After Baseline
Measure Description	According to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1), progressive disease (PD) was defined as at least a 20 percent (%) increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum of the longest diameter recorded since treatment started or the appearance of 1 or more new lesions. For non-target lesions, PD was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-target lesions.

Time Frame	12 months
Safety Issue?	No

Analysis Population Description

Intent to treat (ITT) population included all participants enrolled in the study who received at least 1 dose of treatment.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Percentage of Participants With Disease Progression or Death at 12 Months After Baseline [units: percentage of participants]	42

2. Primary Outcome Measure:

Measure Title	Progression-Free Survival (PFS)
Measure Description	PFS was defined as the time from baseline to the date of first occurrence of disease progression or death. According to RECIST v1.1, PD was defined as at least a 20% increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum of the longest diameter recorded since treatment started or the appearance of 1 or more new lesions. For non-target lesions, PD was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-target lesions. PFS was assessed using Kaplan-Meier method.
Time Frame	Up to 1 year after enrollment of the last participant (maximum up to 27 months)
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Progression-Free Survival (PFS) [units: months] Median (90% Confidence Interval)	12.58 (10.25 to 16.95)

3. Primary Outcome Measure:

Measure Title	Probability of Being Progression Free 12 Months After Baseline
Measure Description	According to RECIST v1.1, PD was defined as at least a 20% increase in the sum of the longest diameter of target lesions, taking as reference the smallest sum of the longest diameter recorded since treatment started or the appearance of 1 or more new lesions. For non-target lesions, PD was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-target lesions.
Time Frame	12 months
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Probability of Being Progression Free 12 Months After Baseline [units: probability of being progression-free] Mean (Standard Error)	0.51 (0.08)

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Died
Measure Description	
Time Frame	Every 8 weeks during treatment, after discontinuation participants were followed for up to 1 year after enrollment of the last participant (maximum up to 27 months)
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Percentage of Participants Who Died [units: percentage of participants]	28

5. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	OS was defined as the time from randomization to the date of death due to any cause. OS was assessed using Kaplan-Meier method.
Time Frame	Every 8 weeks during treatment, after discontinuation participants were followed for up to 1 year after enrollment of the last participant (maximum up to 27 months)
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Overall Survival (OS) [units: months] Mean (Standard Error)	17.48 (1.09)

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Response by Best Overall Response
Measure Description	Tumor response was assessed by the investigator using computed tomography (CT) scans according to RECIST v1.1. Complete response (CR) was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must decrease to normal (short axis less than 10 mm), with no new lesions. Partial response (PR) was defined as greater than or equal to (>=) 30% decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease, and no new lesions. PD is defined in Outcome Measure 1. Stable disease (SD) was defined as not qualifying for CR, PR, or PD. The best overall response achieved from start of treatment until disease progression or end of study is presented.
Time Frame	Baseline up to disease progression or end of study (up to 12 Months)
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Percentage of Participants With a Response by Best Overall Response [units: percentage of participants]	
CR	6
PR	62
SD	12
PD	4
Not estimated	16

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Objective Response
Measure Description	Objective response was defined as the percentage of participants with CR or PR as best overall response by RECIST v1.1. To be assigned the status of PR or CR, changes in tumor measurements were to be confirmed by repeated assessments no less than 4 weeks after the criteria for response were first met. CR was defined as complete disappearance of all target lesions and non-target disease, with exception of nodal disease. All nodes, both target and non-target, must decrease to normal (short axis less than 10 mm), with no new lesions. PR was defined as >=30% decrease under baseline of sum of diameters of all target lesions. The short axis was used in sum for target nodes, while longest diameter was used in sum for all other target lesions. No unequivocal progression of non-target disease, and no new lesions. Participants with no tumor assessment after start of study treatment were considered as non-responders. The percentage of participants with response is presented.
Time Frame	Baseline up to disease progression or end of study (up to 12 Months)
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Percentage of Participants With Objective Response [units: percentage of participants] Number (95% Confidence Interval)	68 (53 to 80)

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving CR, PR, or SD as Best Overall Response
Measure Description	The Disease Control Rate was defined as the percentage of participants who had CR or PR or SD as Best Overall Response achieved within the time between the first drug administration and documented disease progression or end of study. According to RECIST v1.1, CR was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must decrease to normal (short axis less than 10 mm), with no new lesions. PR was defined as >=30% decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease, and no new lesions. SD was defined as not qualifying for CR, PR, or PD.
Time Frame	Baseline up to disease progression or end of study (up to 12 Months)
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	50
Percentage of Participants Achieving CR, PR, or SD as Best Overall Response [units: percentage of participants] Number (95% Confidence Interval)	80 (66 to 90)

9. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Primary and Secondary Resistance
Measure Description	Primary resistance was defined as participants did not reach SD or PR or CR before going to PD. While secondary resistance was defined as participants experienced PD after having reached SD or PR or CR at least once. Please refer to above outcome measures 1 and 6 for definition of CR, PR, SD, and PD.
Time Frame	Baseline up to disease progression (up to 12 Months)
Safety Issue?	No

Analysis Population Description

Analysis population included all participants enrolled in the study who received at least 1 dose of treatment and who had a documented PD response during the study period.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	24
Percentage of Participants With Primary and Secondary Resistance [units: percentage of participants]	
Primary resistance	8.33
Secondary resistance	91.67

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Epidermal Growth Factor Receptor (EGFR) Mutation by Mutation Type
Measure Description	EGFR is a gene in the tumor tissues and mutations in this gene have been linked to a variety of tumors. Presence or absence of EGFR mutation was determined in liquid biopsies by reverse transcriptase-polymerase chain reaction (RT-PCR /Cobas).
Time Frame	Baseline, At progression of disease

Safety Issue?	No

Analysis Population Description

Analysis population included all participants enrolled in the study who received at least 1 dose of treatment and who had samples for EGFR mutation. Here, 'N' (number of participants analyzed) signifies the number of participants analyzed for this outcome measure and 'n' signifies the number of participants analyzed at specified time point.

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Measured Values

	Erlotinib 150 mg
Number of Participants Analyzed	45
Percentage of Participants With Epidermal Growth Factor Receptor (EGFR) Mutation by Mutation Type [units: percentage of participants]	
Baseline: EGFR18 Mutation (n=45)	0.00
Baseline: EGFR19 Codon Deletion Mutation (n=45)	51.11
Baseline: EGFR20 Codon T790M Mutation (n=45)	2.22
Baseline: EGFR21 Codon L585R Mutation (n=45)	15.56
At PD: EGFR18 Mutation (n=18)	0.00
At PD: EGFR19 Codon Deletion Mutation (n=18)	50.00
At PD: EGFR20 Codon T790M Mutation (n=18)	27.78
At PD: EGFR21 Codon L585R Mutation (n=18)	16.67

Reported Adverse Events

Time Frame	Up to 1 year after enrollment of the last participant (maximum up to 27 months)
Additional Description	[Not specified]

Reporting Groups

	Description
Erlotinib 150 mg	Erlotinib 150 mg tablet orally once daily up to end of study (12 months) or until disease progression, unacceptable toxicity or consent withdrawal.

Serious Adverse Events

	Erlotinib 150 mg
	Affected/At Risk (%)
Total	10/50 (20%)
Cardiac disorders	
Cardiac failure acute [A] *	1/50 (2%)
Gastrointestinal disorders	
Dysphagia [A] *	1/50 (2%)
General disorders	
Chest pain [A] *	1/50 (2%)
Infections and infestations	
Pneumonia [A] *	2/50 (4%)
Injury, poisoning and procedural complications	
Hip fracture [A] *	1/50 (2%)
Metabolism and nutrition disorders	
Decreased appetite [A] *	1/50 (2%)
Nervous system disorders	
Convulsion [A] *	1/50 (2%)
Hemiplegia [A] *	1/50 (2%)
Psychiatric disorders	
Confusional state [A] *	1/50 (2%)
Respiratory, thoracic and mediastinal disorders	
Dyspnea [A] *	2/50 (4%)

	Erlotinib 150 mg
	Affected/At Risk (%)
Pneumothorax [A] *	1/50 (2%)
Vascular disorders	
Jugular vein thrombosis [A] *	1/50 (2%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA v14.0

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Erlotinib 150 mg
	Affected/At Risk (%)
Total	46/50 (92%)
Ear and labyrinth disorders	
Vertigo [A] *	4/50 (8%)
Eye disorders	
Conjunctivitis [A] *	11/50 (22%)
Gastrointestinal disorders	
Abdominal pain upper [A] *	4/50 (8%)
Diarrhoea [A] *	26/50 (52%)
Stomatitis [A] *	4/50 (8%)
Vomiting [A] *	4/50 (8%)
General disorders	
Asthenia [A] *	8/50 (16%)
Chest pain [A] *	6/50 (12%)
Fatigue [A] *	4/50 (8%)
Pyrexia [A] *	9/50 (18%)

	Erlotinib 150 mg
	Affected/At Risk (%)
Infections and infestations	
Paronychia [A] *	7/50 (14%)
Injury, poisoning and procedural complications	
Contrast media reaction [A] *	3/50 (6%)
Investigations	
Blood bilirubin increased [A] *	3/50 (6%)
Metabolism and nutrition disorders	
Decreased appetite [A] *	6/50 (12%)
Musculoskeletal and connective tissue disorders	
Back pain [A] *	4/50 (8%)
Muscle spasms [A] *	3/50 (6%)
Musculoskeletal pain [A] *	3/50 (6%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] *	10/50 (20%)
Epistaxis [A] *	3/50 (6%)
Skin and subcutaneous tissue disorders	
Alopecia [A] *	7/50 (14%)
Dermatitis acneiform [A] *	5/50 (10%)
Dry skin [A] *	4/50 (8%)
Pruritus [A] *	10/50 (20%)
Rash [A] *	34/50 (68%)
Skin ulcer [A] *	3/50 (6%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA v14.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

Results Point of Contact:

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