ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 02/05/2015

ClinicalTrials.gov ID: NCT00531934

Study Identification

Unique Protocol ID:	ML20829
Brief Title:	A Study of Management of Tarceva - Induced Rash in Patients With Non-Small Cell Lung Cancer.
Official Title:	A Randomized, Open Label Study to Evaluate the Effect of Doxycycline on Tarceva-induced Skin Rash in Patients With Non-small Cell Lung Cancer After Failure of First Line Chemotherapy
Secondary IDs:	

Study Status

Record Verification:	February 2015
Overall Status:	Completed
Study Start:	October 2007
Primary Completion:	August 2010 [Actual]
Study Completion:	August 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: 2449 Board Name: Ile-de-France III Board Affiliation: Unknown Phone: +33 146 336 867 Email: cpp.iledefrance3@orange.fr
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	France: Agence francaise de securite sanitaire des produits de sante (AFSSAPS)

Study Description

Brief Summary:	This 2 arm study will evaluate the management of Tarceva-induced skin rash in patients with non-small cell lung cancer who have failed first-line chemotherapy for advanced disease. Eligible patients will be randomized to receive a)doxycycline 100mg po daily or b)no preventative treatment; all patients will receive Tarceva 150mg/kg po daily. The anticipated time on study treatment is until disease progression or intolerable toxicity, and the target sample size is 100-500 individuals.
Detailed Description:	

Conditions

Conditions:	Non-Small Cell Lung Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	147 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: Doxycline 100mg po daily Drug: erlotinib [Tarceva] 150mg po daily
Active Comparator: 2	Drug: erlotinib [Tarceva] 150mg po daily

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 75 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, 18-75 years of age;
- confirmed non-small cell lung cancer;
- failure after first line chemotherapy for advanced disease, and scheduled for second line therapy with Tarceva.

Exclusion Criteria:

- rash of any etiology at study entry;
- history of significant heart disease;
- any other malignancies (other than adequately treated squamous cell skin cancer, or in situ cancer of the cervix);
- history of allergic reactions to tetracyclines.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: France
Paris, France, 75674

Antibes, France, 06600

Pontoise, France, 95300

Caen, France, 14076

Bordeaux, France, 33300

Draguignan, France, 83007

Rennes, France, 35033

Perigueux, France, 24000

Metz, France, 57038

Brest, France, 29200

Pierre Benite, France, 69495

Chalon Sur Saone, France, 71100

Limoges, France, 87042

Vannes, France, 56017

Chartres, France, 28018

Nimes, France, 30900

Rouen, France, 76000

Bordeaux, France, 33076

Perpignan, France, 66000

Paris, France, 75116

Paris, France, 75679

GAP, France, 05007

Tours, France, 37044

Gleize, France, 69400

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Erlotinib Plus (+) Doxycycline	Participants received erlotinib 150 milligrams per day (mg/day), tablets, orally (PO) until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Overall Study

	Erlotinib Plus (+) Doxycycline	Erlotinib
Started	73	74
Completed	7	11
Not Completed	66	63
Adverse Event	4	8
Progression	52	42
Death	7	10
Withdrawal by Subject	1	1
Not specified	2	2

Baseline Characteristics

Analysis Population Description

Intent-to-Treat population (ITT): all randomized participants who received at least

1 dose of erlotinib.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Baseline Measures

	Erlotinib + Doxycycline	Erlotinib	Total
Number of Participants	73	74	147
Age, Continuous [units: years] Mean (Standard Deviation)	63.5 (10.6)	64.2 (11.1)	63.8 (10.8)
Gender, Male/Female [units: participants]			
Female	25	24	49
Male	48	50	98

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With at Least One Skin Rash (Folliculitis) of Any Grade During the First 4 Months of Treatment
Measure Description	Description of skin rash (folliculitis, including erythema, papulo-pustules, nodule, and crust) was according to Common Terminology Criteria for Adverse Events (CTCAE) version 3 scale. Medical pictures of the face (front and sides views) systematically, and of any region presenting with skin lesions were obtained. The pictures were reviewed by a centralized committee of evaluation.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	Yes

Analysis Population Description

ITT population; data for 1 participant in the erlotinib treatment group were missing.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	73
Percentage of Participants With at Least One Skin Rash (Folliculitis) of Any Grade During the First 4 Months of Treatment [units: percentage of participants]	71.2	80.8

Statistical Analysis 1 for Percentage of Participants With at Least One Skin Rash (Folliculitis) of Any Grade During the First 4 Months of Treatment

Statistical Analysis Overview	Comparison Groups	Erlotinib + Doxycycline, Erlotinib
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.175
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Number of Skin Rash (Folliculitis) Events During the First 4 Months of Treatment
Measure Description	A cutaneous rash as folliculitis can be defined with several types including erythema, papulo-pustular and nodules.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Number of Skin Rash (Folliculitis) Events During the First 4 Months of Treatment [units: rash events]	57	62

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Skin Rash (Folliculitis) During the First 4 Months of Treatment By Type
Measure Description	A cutaneous rash as folliculitis can be defined with several types including erythema, papulo-pustule, nodule, and crust.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants With Skin Rash (Folliculitis) During the First 4 Months of Treatment By Type [units: percentage of participants]		
Erythema	55.8	70.7
Papulo-pustule	65.4	72.4
Nodule	1.9	0
Crust	9.6	25.9

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Skin Rash (Folliculitis) During the First 4 Months of Treatment By Maximal Intensity
Measure Description	Intensity of skin rashes was classified according to CTCAE grading. Grade 1 equals (=) Macular or papular eruption or erythema without associated symptoms; Grade 2=Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering less than (<)50 percent (%) of body surface area (BSA); Grade 3=Severe, generalized erythroderma or macular, papular, or vesicular eruption; desquamation.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description

ITT population; only participants with an adverse event of skin rash (folliculitis) during the first 4 months were included in the analysis.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	52	59
Percentage of Participants With Skin Rash (Folliculitis) During the First 4 Months of Treatment By Maximal Intensity [units: percentage of participants]		
Grade 1	61.5	18.6
Grade 2	34.6	62.7
Grade 3	3.8	18.6

Statistical Analysis 1 for Percentage of Participants With Skin Rash (Folliculitis) During the First 4 Months of Treatment By Maximal Intensity

Statistical Analysis Overview	Comparison Groups	Erlotinib + Doxycycline, Erlotinib
	Comments	Erlotinib + doxycycline vs Erlotinib: Grade 3 intensity skin rash (folliculitis)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With at Least One Skin Rash (Folliculitis) of Any Grade After the First 4 Months of Treatment
Measure Description	
Time Frame	Months 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants With at Least One Skin Rash (Folliculitis) of Any Grade After the First 4 Months of Treatment [units: percentage of participants]	2.7	1.4

6. Secondary Outcome Measure:

Measure Title	Number of Skin Rash (Folliculitis) Events After the First 4 Months of Treatment
Measure Description	A cutaneous rash as folliculitis can be defined with several types including erythema, papulo-pustular and nodules.
Time Frame	Months 7, 10, and 12
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	73

	Erlotinib + Doxycycline	Erlotinib
Number of Skin Rash (Folliculitis) Events After the First 4 Months of Treatment [units: rash events]	2	1

7. Secondary Outcome Measure:

Measure Title	Number of Participants With Skin Rash (Folliculitis) After the First 4 Months of Treatment By Type
Measure Description	A cutaneous rash as folliculitis can be defined with several types including erythema, papulo-pustule, nodule, and crust.
Time Frame	Months 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Number of Participants With Skin Rash (Folliculitis) After the First 4 Months of Treatment By Type [units: participants]		
Erythema	1	1
Papulo-pustule	1	1
Nodule	0	0
Crust	0	0

8. Secondary Outcome Measure:

Measure Title	Number of Participants With Skin Rash (Folliculitis) After the First 4 Months of Treatment By Intensity
Measure Description	Intensity of skin rashes was classified according to CTCAE grading. Grade 1=Macular or papular eruption or erythema without associated symptoms; Grade 2=Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of BSA; Grade 3=Severe, generalized erythroderma or macular, papular, or vesicular eruption; desquamation.
Time Frame	Months 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Number of Participants With Skin Rash (Folliculitis) After the First 4 Months of Treatment By Intensity [units: participants]		
Initial intensity: Grade 1	2	1
Maximal intensity: Grade 1	2	1

9. Secondary Outcome Measure:

Measure Title	Time Free From Skin Rash (Folliculitis) During the First 4 Months of Treatment - Number of Participants With an Event
Measure Description	Period without occurrence was determined as the number of days from the first dose of medication until the first appearance of folliculitis, analyzed using Kaplan-Meier analysis.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4

Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Time Free From Skin Rash (Folliculitis) During the First 4 Months of Treatment - Number of Participants With an Event [units: participants]	52	59

10. Secondary Outcome Measure:

Measure Title	Time Free From Skin Rash (Folliculitis) During the First 4 Months of Treatment - Time to Event
Measure Description	Period without occurrence was determined as the number of days from the first dose of medication until the first appearance of folliculitis, analyzed using Kaplan-Meier analysis.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.

	Description
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Time Free From Skin Rash (Folliculitis) During the First 4 Months of Treatment - Time to Event [units: days] Median (95% Confidence Interval)	14 (13 to 22)	13 (8 to 16)

Statistical Analysis 1 for Time Free From Skin Rash (Folliculitis) During the First 4 Months of Treatment - Time to Event

Statistical Analysis Overview	Comparison Groups	Erlotinib + Doxycycline, Erlotinib
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.143
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.763
	Confidence Interval	(2-Sided) 95% 0.525 to 1.109
	Estimation Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants Estimated to be Event Free at 4 Months
Measure Description	Percentage of participants estimated to be without skin rash (folliculitis) at 4 months.

Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants Estimated to be Event Free at 4 Months [units: percentage of participants]	24.7	11.2

12. Secondary Outcome Measure:

Measure Title	Time Free From Skin Rash (Folliculitis) During the Whole Treatment Period - Number of Participants With an Event
Measure Description	Period without occurrence was determined as the number of days from the first dose of medication until the first appearance of folliculitis, analyzed using Kaplan-Meier analysis.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.

	Description
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	73
Time Free From Skin Rash (Folliculitis) During the Whole Treatment Period - Number of Participants With an Event [units: participants]	53	59

13. Secondary Outcome Measure:

Measure Title	Time Free From Skin Rash (Folliculitis) During the Whole Treatment Period - Time to Event
Measure Description	Period without occurrence was determined as the number of days from the first dose of medication until the first appearance of folliculitis, analyzed using Kaplan-Meier analysis.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	73
Time Free From Skin Rash (Folliculitis) During the Whole Treatment Period - Time to Event [units: days]	14 (13 to 22)	13 (8 to 16)

	Erlotinib + Doxycycline	Erlotinib
Median (95% Confidence Interval)		

Statistical Analysis 1 for Time Free From Skin Rash (Folliculitis) During the Whole Treatment Period - Time to Event

Statistical Analysis Overview	Comparison Groups	Erlotinib + Doxycycline, Erlotinib
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.153
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.769
	Confidence Interval	(2-Sided) 95% 0.529 to 1.116
	Estimation Comments	[Not specified]

14. Secondary Outcome Measure:

Measure Title	Percentage of Participants Estimated to be Event Free at 12 Months
Measure Description	Percentage of participants estimated to be without skin rash (folliculitis) at 12 months.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants Estimated to be Event Free at 12 Months [units: percentage of participants]	19.8	11.2

15. Secondary Outcome Measure:

Measure Title	Duration of Skin Rash (Folliculitis) During the First 4 Months of Treatment
Measure Description	If the cutaneous rash was ongoing at the last visit or Month 4, the duration of cutaneous rash was calculated between start of folliculitis and Visit Month 4 or premature withdrawal visit or death.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description

ITT Population; only participants with an event (folliculitis) were included in the analysis.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	57	61

	Erlotinib + Doxycycline	Erlotinib
Duration of Skin Rash (Folliculitis) During the First 4 Months of Treatment [units: days] Mean (Standard Deviation)	59.6 (35.9)	60.6 (33.5)

16. Secondary Outcome Measure:

Measure Title	Duration of Skin Rash (Folliculitis) During the Whole Treatment Period
Measure Description	If the end of cutaneous rash was missing, the duration of cutaneous rash was calculated between start of folliculitis and last evaluation date.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT Population; only participants with an event (folliculitis) were included in the analysis.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	59	62
Duration of Skin Rash (Folliculitis) During the Whole Treatment Period [units: days] Median (Standard Deviation)	86.7 (81.1)	99.3 (90.5)

17. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Other Skin Lesions of Any Grade During the First 4 Months of Treatment

Measure Description	Other skin lesions included presence or absence of xerosis and paronychia.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants With Other Skin Lesions of Any Grade During the First 4 Months of Treatment [units: percentage of participants]	39.7	42.5

18. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Other Skin Lesions During the First 4 Months of Treatment By Type
Measure Description	Other skin lesions included xerosis and paronychia.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants With Other Skin Lesions During the First 4 Months of Treatment By Type [units: percentage of participants]		
Xerosis	37.0	41.1
Paronychia	6.8	8.2

19. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Other Skin Lesions During the First 4 Months of Treatment By Maximal Intensity
Measure Description	Other skin lesions included xerosis and paronychia. Intensity was classified according to CTCAE grading. Grade 1=Macular or papular eruption or erythema without associated symptoms; Grade 2=Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of BSA; Grade 3=Severe, generalized erythroderma or macular, papular, or vesicular eruption; desquamation; Grade 4=Generalized exfoliative, ulcerative, or bullous dermatitis. If a participant had several skin lesions, the maximal intensity was taken into account.
Time Frame	Days 0, 14, 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description

ITT population; only participants with an adverse event classified as other skin lesion during the first 4 months were included in the analysis.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	29	31
Percentage of Participants With Other Skin Lesions During the First 4 Months of Treatment By Maximal Intensity [units: percentage of participants]		
Grade 1	69.0	29.0
Grade 2	24.1	51.6
Grade 3	6.9	16.1
Grade 4	0	3.2

Statistical Analysis 1 for Percentage of Participants With Other Skin Lesions During the First 4 Months of Treatment By Maximal Intensity

Statistical Analysis Overview	Comparison Groups	Erlotinib + Doxycycline, Erlotinib
	Comments	Erlotinib + doxycycline vs Erlotinib: Grade 3
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.003
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

20. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Erlotinib Dose Reduction by Reason for Reduction
Measure Description	Erlotinib dose adjustment was done in case of toxicity occurrence. Keratitis, diarrhea, interstitial lung disease, and other toxic occurrences determined erlotinib dose reduction. If erlotinib was previously discontinued for skin rash or diarrhea of Grade 2 and if these symptoms of Grade 2 recurred OR if the symptoms were intolerable for the participants, erlotinib was discontinued until recovery/Grade 1 then the dose was reduced of one level of 50 mg.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population; only participants that discontinued or interrupted erlotinib were included in the analysis.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	23	32
Percentage of Participants With Erlotinib Dose Reduction by Reason for Reduction [units: percentage of participants]		
Adverse event	80.0	85.7
Investigator's decision	0	2.4
Other	20.0	11.9

21. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Doxycycline Dose Reduction by Reason for Reduction
Measure Description	Occurrence of folliculitis-type skin rash of Grade greater than or equal to (≥)2 led to dose modification. Continuation of treatment with doxycycline after occurrence of folliculitis-type skin rash of Grade ≥2 was upon the investigator’s opinion.

Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population; only participants that discontinued or interrupted doxycycline were included in the analysis.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	8	0
Percentage of Participants With Doxycycline Dose Reduction by Reason for Reduction [units: percentage of participants]		
Adverse event	50.0	
Other	50.0	

22. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Global Disease Control by Visit
Measure Description	Disease control was determined according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria for evaluation and was defined as participants with either complete response (CR), partial response (PR), or stable disease (SD).
Time Frame	Months 2, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT population; number (n) = number of participants analyzed for the specified parameter at a given visit.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	34	33
Percentage of Participants With Global Disease Control by Visit [units: percentage of participants]		
Month 2 (n=34,33)	88.2	93.9
Month 4 (n=19,25)	89.5	80.0
Month 7 (n=11,17)	72.7	76.5
Month 10 (n=7,12)	100.0	66.7
Month 12 (n=7,10)	71.4	40.0

23. Secondary Outcome Measure:

Measure Title	Percentage of Participants by Best Global Response Under Treatment
Measure Description	Response was determined according to the RECIST criteria for evaluation and was defined as participants with either CR, PR, SD, or progression. No CR was reported.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	58	58
Percentage of Participants by Best Global Response Under Treatment [units: percentage of participants]		
PR	15.5	10.3
SD	36.2	48.3
Progression	48.3	41.4

24. Secondary Outcome Measure:

Measure Title	Progression-Free Survival (PFS) - Percentage of Participants With an Event
Measure Description	PFS was defined by the time between first intake of treatment with erlotinib and disease progression or death for any cause; estimated using Kaplan-Meier method.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Progression-Free Survival (PFS) - Percentage of Participants With an Event [units: percentage of participants]	91.8	87.8

25. Secondary Outcome Measure:

Measure Title	Progression-Free Survival (PFS) - Time to Event
Measure Description	PFS was defined by the time between first intake of treatment with erlotinib and disease progression or death for any cause; estimated using Kaplan-Meier method.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Progression-Free Survival (PFS) - Time to Event [units: days] Median (95% Confidence Interval)	63.0 (56.0 to 107.0)	70.0 (56.0 to 107.0)

26. Secondary Outcome Measure:

Measure Title	Percentage of Participants Estimated to be Progression Free at 4 and 12 Months
Measure Description	
Time Frame	Months 4 and 12
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants Estimated to be Progression Free at 4 and 12 Months [units: percentage of participants]		
4 Months	30.1	31.0
12 Months	6.3	10.8

27. Secondary Outcome Measure:

Measure Title	Overall Survival (OS) - Percentage of Participants With an Event
Measure Description	OS was defined by the time between first intake of treatment with erlotinib and death for any cause; analyzed using Kaplan-Meier method.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Overall Survival (OS) - Percentage of Participants With an Event [units: percentage of participants]	71.2	67.6

28. Secondary Outcome Measure:

Measure Title	Overall Survival (OS) - Time to Event
Measure Description	OS was defined by the time between first intake of treatment with erlotinib and death for any cause; analyzed using Kaplan-Meier method.
Time Frame	Days 0, 14, 28 and Months 2, 3, 4, 7, 10, and 12
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Overall Survival (OS) - Time to Event [units: days] Median (95% Confidence Interval)	227.0 (153.0 to 282.0)	251.0 (152.0 to 336.0)

29. Secondary Outcome Measure:

Measure Title	Percentage of Participants Estimated to be Alive at 4 and 12 Months
Measure Description	
Time Frame	Months 4 and 12
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	73	74
Percentage of Participants Estimated to be Alive at 4 and 12 Months [units: percentage of participants]		
4 Months	68.5	69.7
12 Months	27.1	33.5

30. Secondary Outcome Measure:

Measure Title	Dermatology Life Quality Index (DLQI) Global Score
Measure Description	Quality of life was assessed by participant's responses to a DLQI questionnaire. The DLQI is a 10-item questionnaire assessing quality of life; questions were assessed on a 4-point scale (0=not at all; 1=a little; 2=a lot; and 3=very much). The DLQI was calculated by summing the score of each question resulting in a maximum of 30 (extremely large effect on participant's life) and a minimum of 0 (no effect at all on participant's life). The higher the score, the more quality of life is impaired. Analysis was performed by visit well as at the last available value after baseline (Endpoint); change from baseline to endpoint was also determined.
Time Frame	Baseline, Days 14 and 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description

ITT Population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	67	69
Dermatology Life Quality Index (DLQI) Global Score [units: units on a scale] Mean (Standard Deviation)		
Baseline (n=67,69)	0.2 (0.5)	0.2 (0.6)
Day 14 (n=63,62)	1.7 (3.2)	3.7 (4.3)
Day 28 (n=60,56)	1.7 (2.5)	3.4 (4.0)
Month 2 (n=35,37)	2.3 (4.1)	4.3 (5.3)
Month 3 (n=29,27)	1.7 (2.7)	3.2 (3.7)
Month 4 (n=19,24)	1.6 (3.0)	2.6 (3.5)
Endpoint (n=65,63)	2.0 (3.3)	3.4 (4.8)
Change at Endpoint (n=35,37)	1.9 (3.3)	3.2 (4.8)

31. Secondary Outcome Measure:

Measure Title	Percentage of Participants by DLQI Global Score Classification of Disease Effect on Quality of Life
Measure Description	Quality of life was assessed by participant's responses to a DLQI questionnaire. The DLQI is a 10-item questionnaire assessing quality of life; questions were assessed on a 4-point scale (0=not at all; 1=a little; 2=a lot; and 3=very much). The DLQI was calculated by summing the score of each question resulting in a maximum of 30 (extremely large effect on participant's life) and a minimum of 0 (no effect at all on participant's life). The higher the score, the more quality of life is impaired. The DLQI global score was classified into 5 levels: 0-1 (no effect at all), 2-5 (small effect), 6-10 (moderate effect), 11-20 (very large effect) and 21-30 (extremely large effect).
Time Frame	Baseline, Days 14 and 28 and Months 2, 3, and 4
Safety Issue?	No

Analysis Population Description

ITT Population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	67	69
Percentage of Participants by DLQI Global Score Classification of Disease Effect on Quality of Life [units: percentage of participants]		
Baseline, no effect (n=67,69)	98.5	97.1
Baseline, small effect (n=67,69)	1.5	2.9
Day 14, no effect (n=63,62)	69.8	41.9
Day 14, small effect (n=63,62)	27.0	30.6
Day 14, moderate effect (n=63,62)	0.0	21.0

	Erlotinib + Doxycycline	Erlotinib
Day 14, very large effect (n=63,62)	1.6	6.5
Day 14, extremely large effect (n=63,62)	1.6	0.0
Day 28, no effect (n=60,56)	66.7	41.1
Day 28, small effect (n=60,56)	25.0	35.7
Day 28, moderate effect (n=60,56)	8.3	19.6
Day 28, very large effect (n=60,56)	0.0	1.8
Day 28, extremely large effect (n=60,56)	0.0	1.8
Month 2, no effect (n=35,37)	65.7	40.5
Month 2, small effect (n=35,37)	22.9	27.0
Month 2, moderate effect (n=35,37)	5.7	21.6
Month 2, very large effect (n=35,37)	5.7	8.1
Month 2, extremely large effect (n=35,37)	0.0	2.7
Month 3, no effect (n=29,27)	69.0	37.0
Month 3, small effect (n=29,27)	27.6	44.4
Month 3, moderate effect (n=29,27)	0.0	11.1
Month 3, very large effect (n=29,27)	3.4	7.4
Month 4, no effect (n=19,24)	78.9	50.0
Month 4, small effect (n=19,24)	15.8	41.7
Month 4, very large effect (n=19,24)	5.3	8.3

32. Secondary Outcome Measure:

Measure Title	Quality of Life Score as Assessed by Visual Analog Scale (VAS)
Measure Description	Quality of life was assessed by participant's responses to a VAS questionnaire - (evaluation of satisfaction with skin status). VAS was measured on a 100 millimeter (mm) scale where 0 = not at all satisfied and 100 = very satisfied. Participants were asked to mark the line corresponding to their satisfaction at each visit and the distance from the left edge was measured. A negative change from baseline indicates improvement. Analysis was performed by visit well as at the last available value after baseline (Endpoint).
Time Frame	Baseline, Days 14 and 28, and Months 2, 3, and 4

Safety Issue?	No

Analysis Population Description

ITT population; n=number of participants assessed for the specified parameter at a given visit.

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Measured Values

	Erlotinib + Doxycycline	Erlotinib
Number of Participants Analyzed	64	68
Quality of Life Score as Assessed by Visual Analog Scale (VAS) [units: mm] Mean (Standard Deviation)		
Baseline (n=64,68)	81.4 (23.7)	87.8 (19.6)
Day 14 (n=62,63)	68.8 (26.6)	51.0 (34.5)
Change at Day 14 (n=59,61)	-16.2 (28.5)	-39.2 (37.8)
Day 28 (n=59,56)	66.5 (27.2)	54.8 (27.0)
Change at Day 28 (n=55,54)	-15.5 (28.8)	-35.1 (27.8)
Month 2 (n=36,36)	68.9 (22.8)	52.6 (27.4)
Month 3 (n=28,27)	63.5 (21.4)	56.1 (31.7)
Month 4 (n=18,24)	71.8 (20.9)	59.9 (29.7)
Endpoint (n=65,64)	64.0 (26.6)	58.3 (30.8)
Change at Endpoint (n=60,62)	-18.1 (27.7)	-30.4 (31.4)

Reported Adverse Events

Time Frame	Adverse events (AEs) were recorded continuously until 30 days after the last treatment administration.
Additional Description	[Not specified]

Reporting Groups

	Description
Erlotinib + Doxycycline	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity and doxycycline 100 mg/day, tablets, PO for the first 4 months of the study; after this period it was the investigator's choice to continue treatment with doxycycline.
Erlotinib	Participants received erlotinib 150 mg/day, tablets, PO until progression or unacceptable toxicity.

Serious Adverse Events

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	18/73 (24.66%)	24/74 (32.43%)
Cardiac disorders		
Cardiac failure [A] *	1/73 (1.37%)	0/74 (0%)
Myocardial infarction [A] *	1/73 (1.37%)	0/74 (0%)
Myocardial ischaemia [A] *	1/73 (1.37%)	0/74 (0%)
Pericarditis [A] *	1/73 (1.37%)	0/74 (0%)
Gastrointestinal disorders		
Abdominal pain [A] *	2/73 (2.74%)	0/74 (0%)
Colonic obstruction [A] *	1/73 (1.37%)	0/74 (0%)
Constipation [A] *	0/73 (0%)	1/74 (1.35%)
Diarrhoea [A] *	2/73 (2.74%)	1/74 (1.35%)
Nausea [A] *	0/73 (0%)	1/74 (1.35%)
Oesophageal achalasia [A] *	0/73 (0%)	1/74 (1.35%)
Rectal haemorrhage [A] *	1/73 (1.37%)	0/74 (0%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Vomiting [A] *	0/73 (0%)	1/74 (1.35%)
General disorders		
Chest pain [A] *	0/73 (0%)	1/74 (1.35%)
Death [A] *	1/73 (1.37%)	1/74 (1.35%)
General physical health deterioration [A] *	4/73 (5.48%)	6/74 (8.11%)
Malaise [A] *	0/73 (0%)	1/74 (1.35%)
Pain [A] *	0/73 (0%)	1/74 (1.35%)
Xerosis [A] *	0/73 (0%)	1/74 (1.35%)
Infections and infestations		
Sepsis [A] *	0/73 (0%)	4/74 (5.41%)
Staphylococcal skin infection [A] *	1/73 (1.37%)	0/74 (0%)
Injury, poisoning and procedural complications		
Overdose [A] *	0/73 (0%)	1/74 (1.35%)
Metabolism and nutrition disorders		
Dehydration [A] *	0/73 (0%)	1/74 (1.35%)
Hyponatraemia [A] *	0/73 (0%)	1/74 (1.35%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	0/73 (0%)	1/74 (1.35%)
Rhabdomyolysis [A] *	0/73 (0%)	1/74 (1.35%)
Nervous system disorders		
Headache [A] *	0/73 (0%)	1/74 (1.35%)
Intracranial pressure increased [A] *	1/73 (1.37%)	0/74 (0%)
Sciatica [A] *	0/73 (0%)	1/74 (1.35%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Respiratory, thoracic and mediastinal disorders		
Bronchitis chronic [A] *	0/73 (0%)	1/74 (1.35%)
Chronic obstructive pulmonary disease [A] *	0/73 (0%)	1/74 (1.35%)
Dyspnoea [A] *	1/73 (1.37%)	1/74 (1.35%)
Lung disorder [A] *	1/73 (1.37%)	1/74 (1.35%)
Pulmonary embolism [A] *	0/73 (0%)	3/74 (4.05%)
Skin and subcutaneous tissue disorders		
Folliculitis [A] *	0/73 (0%)	1/74 (1.35%)
Vascular disorders		
Phlebitis [A] *	0/73 (0%)	1/74 (1.35%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, CTCAE (3.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	71/73 (97.26%)	69/74 (93.24%)
Blood and lymphatic system disorders		
Anaemia [A] *	4/73 (5.48%)	5/74 (6.76%)
Neutropenia [A] *	0/73 (0%)	1/74 (1.35%)
Cardiac disorders		
Cardiac tamponade [A] *	1/73 (1.37%)	0/74 (0%)
Sinus tachycardia [A] *	0/73 (0%)	1/74 (1.35%)
Tachycardia [A] *	1/73 (1.37%)	1/74 (1.35%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Ear and labyrinth disorders		
Cerumen impaction [A] *	0/73 (0%)	1/74 (1.35%)
Ear haemorrhage [A] *	0/73 (0%)	1/74 (1.35%)
Vertigo [A] *	1/73 (1.37%)	1/74 (1.35%)
Endocrine disorders		
Adrenal insufficiency [A] *	0/73 (0%)	1/74 (1.35%)
Eye disorders		
Conjunctivitis [A] *	2/73 (2.74%)	6/74 (8.11%)
Dry eye [A] *	2/73 (2.74%)	1/74 (1.35%)
Eye irritation [A] *	1/73 (1.37%)	0/74 (0%)
Eye pain [A] *	1/73 (1.37%)	0/74 (0%)
Eye pruritus [A] *	1/73 (1.37%)	1/74 (1.35%)
Growth of eyelashes [A] *	0/73 (0%)	2/74 (2.7%)
Keratitis [A] *	0/73 (0%)	1/74 (1.35%)
Lacrimation increased [A] *	0/73 (0%)	1/74 (1.35%)
Ocular hyperaemia [A] *	0/73 (0%)	1/74 (1.35%)
Visual distrubance [A] *	1/73 (1.37%)	0/74 (0%)
Gastrointestinal disorders		
Abdominal pain [A] *	5/73 (6.85%)	2/74 (2.7%)
Abdominal pain upper [A] *	0/73 (0%)	3/74 (4.05%)
Abdominal rigidity [A] *	0/73 (0%)	1/74 (1.35%)
Aerophagia [A] *	0/73 (0%)	1/74 (1.35%)
Aphthous stomatitis [A] *	2/73 (2.74%)	3/74 (4.05%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Constipation [A] *	8/73 (10.96%)	5/74 (6.76%)
Diarrhoea [A] *	26/73 (35.62%)	34/74 (45.95%)
Dry mouth [A] *	1/73 (1.37%)	0/74 (0%)
Dyspepsia [A] *	1/73 (1.37%)	0/74 (0%)
Dysphagia [A] *	1/73 (1.37%)	0/74 (0%)
Faecaloma [A] *	0/73 (0%)	1/74 (1.35%)
Gastrointestinal disorder [A] *	4/73 (5.48%)	0/74 (0%)
Gastrooesophageal reflux disease [A] *	3/73 (4.11%)	2/74 (2.7%)
Gingival bleeding [A] *	0/73 (0%)	1/74 (1.35%)
Gingival hypertrophy [A] *	0/73 (0%)	1/74 (1.35%)
Gingival pain [A] *	0/73 (0%)	1/74 (1.35%)
Gingivitis [A] *	0/73 (0%)	1/74 (1.35%)
Glossitis [A] *	0/73 (0%)	1/74 (1.35%)
Haematemesis [A] *	0/73 (0%)	1/74 (1.35%)
Haemorrhoids [A] *	1/73 (1.37%)	1/74 (1.35%)
Hiatus hernia [A] *	1/73 (1.37%)	0/74 (0%)
Inguinal hernia [A] *	0/73 (0%)	1/74 (1.35%)
Nausea [A] *	8/73 (10.96%)	8/74 (10.81%)
Salivary hypersecretion [A] *	0/73 (0%)	1/74 (1.35%)
Stomatitis [A] *	8/73 (10.96%)	1/74 (1.35%)
Subileus [A] *	1/73 (1.37%)	0/74 (0%)
Vomiting [A] *	10/73 (13.7%)	8/74 (10.81%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
General disorders		
Asthenia [A] *	5/73 (6.85%)	9/74 (12.16%)
Catheter site inflammation [A] *	1/73 (1.37%)	0/74 (0%)
Chest pain [A] *	0/73 (0%)	2/74 (2.7%)
Fatigue [A] *	1/73 (1.37%)	1/74 (1.35%)
General physical health deterioration [A] *	0/73 (0%)	4/74 (5.41%)
Hyperthermia [A] *	1/73 (1.37%)	0/74 (0%)
Malaise [A] *	1/73 (1.37%)	0/74 (0%)
Oedema peripheral [A] *	3/73 (4.11%)	1/74 (1.35%)
Pain [A] *	0/73 (0%)	2/74 (2.7%)
Pyrexia [A] *	1/73 (1.37%)	1/74 (1.35%)
Xerosis [A] *	28/73 (38.36%)	30/74 (40.54%)
Hepatobiliary disorders		
Cholestasis [A] *	1/73 (1.37%)	0/74 (0%)
Cytolytic hepatitis [A] *	1/73 (1.37%)	3/74 (4.05%)
Hyperbilirubinaemia [A] *	0/73 (0%)	1/74 (1.35%)
Infections and infestations		
Abscess [A] *	1/73 (1.37%)	0/74 (0%)
Bronchitis [A] *	2/73 (2.74%)	2/74 (2.7%)
Bronchitis viral [A] *	1/73 (1.37%)	0/74 (0%)
Bronchopulmonary aspergillosis [A] *	1/73 (1.37%)	0/74 (0%)
Central line infection [A] *	1/73 (1.37%)	0/74 (0%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Conjunctivitis infective [A] *	1/73 (1.37%)	0/74 (0%)
Cystitis [A] *	1/73 (1.37%)	0/74 (0%)
Ear infection [A] *	1/73 (1.37%)	0/74 (0%)
Fungal infection [A] *	0/73 (0%)	1/74 (1.35%)
Fungal skin infection [A] *	2/73 (2.74%)	2/74 (2.7%)
Gastroenteritis [A] *	1/73 (1.37%)	2/74 (2.7%)
Herpes zoster [A] *	1/73 (1.37%)	0/74 (0%)
Influenza [A] *	0/73 (0%)	1/74 (1.35%)
Lung infection [A] *	0/73 (0%)	2/74 (2.7%)
Nasopharyngitis [A] *	1/73 (1.37%)	0/74 (0%)
Oral fungal infection [A] *	3/73 (4.11%)	1/74 (1.35%)
Oral herpes [A] *	1/73 (1.37%)	0/74 (0%)
Pertussis [A] *	0/73 (0%)	1/74 (1.35%)
Sinusitis [A] *	1/73 (1.37%)	0/74 (0%)
Staphylococcal infection [A] *	1/73 (1.37%)	1/74 (1.35%)
Tonsillitis [A] *	1/73 (1.37%)	0/74 (0%)
Urinary tract infection [A] *	0/73 (0%)	1/74 (1.35%)
Vaginal infection [A] *	1/73 (1.37%)	0/74 (0%)
Injury, poisoning and procedural complications		
Eschar [A] *	0/73 (0%)	2/74 (2.7%)
Rib fracture [A] *	0/73 (0%)	1/74 (1.35%)
Traumatic haematoma [A] *	1/73 (1.37%)	0/74 (0%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Investigations		
Blood alkaline phosphatase increased [A] *	0/73 (0%)	1/74 (1.35%)
Blood bilirubin increased [A] *	4/73 (5.48%)	0/74 (0%)
Gamma-glutamyltransferase increased [A] *	0/73 (0%)	1/74 (1.35%)
Liver function test abnormal [A] *	0/73 (0%)	1/74 (1.35%)
Weight decreased [A] *	1/73 (1.37%)	4/74 (5.41%)
White blood cell count increased [A] *	0/73 (0%)	1/74 (1.35%)
Metabolism and nutrition disorders		
Anorexia [A] *	5/73 (6.85%)	9/74 (12.16%)
Dehydration [A] *	0/73 (0%)	2/74 (2.7%)
Diabetes mellitus inadequate control [A] *	1/73 (1.37%)	0/74 (0%)
Hypokalaemia [A] *	3/73 (4.11%)	0/74 (0%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	1/73 (1.37%)	1/74 (1.35%)
Back pain [A] *	3/73 (4.11%)	2/74 (2.7%)
Bone pain [A] *	2/73 (2.74%)	0/74 (0%)
Groin pain [A] *	1/73 (1.37%)	0/74 (0%)
Muscular weakness [A] *	0/73 (0%)	1/74 (1.35%)
Myalgia [A] *	2/73 (2.74%)	2/74 (2.7%)
Neck pain [A] *	0/73 (0%)	1/74 (1.35%)
Pain in extremity [A] *	1/73 (1.37%)	1/74 (1.35%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma [A] *	1/73 (1.37%)	0/74 (0%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Nervous system disorders		
Aphonia [A] *	0/73 (0%)	1/74 (1.35%)
Dementia [A] *	1/73 (1.37%)	0/74 (0%)
Dysarthria [A] *	0/73 (0%)	1/74 (1.35%)
Dysgeusia [A] *	1/73 (1.37%)	0/74 (0%)
Epiduritis [A] *	1/73 (1.37%)	0/74 (0%)
Facial neuralgia [A] *	0/73 (0%)	1/74 (1.35%)
Headache [A] *	1/73 (1.37%)	3/74 (4.05%)
Paraesthesia [A] *	0/73 (0%)	1/74 (1.35%)
Parosmia [A] *	1/73 (1.37%)	0/74 (0%)
Sciatica [A] *	1/73 (1.37%)	0/74 (0%)
Syncope [A] *	0/73 (0%)	1/74 (1.35%)
Transient ischaemic attack [A] *	2/73 (2.74%)	0/74 (0%)
Vocal cord paralysis [A] *	0/73 (0%)	1/74 (1.35%)
Psychiatric disorders		
Anxiety [A] *	0/73 (0%)	2/74 (2.7%)
Confusional state [A] *	0/73 (0%)	1/74 (1.35%)
Depression [A] *	1/73 (1.37%)	3/74 (4.05%)
Insomnia [A] *	1/73 (1.37%)	0/74 (0%)
Renal and urinary disorders		
Renal failure [A] *	1/73 (1.37%)	0/74 (0%)
Renal failure acute [A] *	0/73 (0%)	1/74 (1.35%)
Reproductive system and breast disorders		

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Vulvovaginal dryness [A] *	0/73 (0%)	1/74 (1.35%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	1/73 (1.37%)	1/74 (1.35%)
Dysphonia [A] *	1/73 (1.37%)	0/74 (0%)
Epistaxis [A] *	1/73 (1.37%)	4/74 (5.41%)
Laryngeal disorder [A] *	0/73 (0%)	1/74 (1.35%)
Pulmonary embolism [A] *	0/73 (0%)	1/74 (1.35%)
Rhinitis [A] *	1/73 (1.37%)	1/74 (1.35%)
Rhinorrhoea [A] *	1/73 (1.37%)	0/74 (0%)
Skin and subcutaneous tissue disorders		
Alopecia [A] *	2/73 (2.74%)	3/74 (4.05%)
Folliculitis [A] *	53/73 (72.6%)	58/74 (78.38%)
Hyperkeratosis [A] *	1/73 (1.37%)	0/74 (0%)
Hypertrichosis [A] *	1/73 (1.37%)	2/74 (2.7%)
Ingrowing nail [A] *	1/73 (1.37%)	0/74 (0%)
Intertrigo [A] *	0/73 (0%)	2/74 (2.7%)
Nail disorder [A] *	1/73 (1.37%)	2/74 (2.7%)
Paronychia [A] *	5/73 (6.85%)	6/74 (8.11%)
Skin discolouration [A] *	0/73 (0%)	1/74 (1.35%)
Vascular disorders		
Deep vein thrombosis [A] *	1/73 (1.37%)	0/74 (0%)
Haematoma [A] *	0/73 (0%)	1/74 (1.35%)

	Erlotinib + Doxycycline	Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Hypotension [A] *	0/73 (0%)	1/74 (1.35%)
Orthostatic hypotension [A] *	0/73 (0%)	1/74 (1.35%)
Periphlebitis [A] *	1/73 (1.37%)	0/74 (0%)
Phlebitis [A] *	0/73 (0%)	1/74 (1.35%)
Venous thrombosis limb [A] *	0/73 (0%)	1/74 (1.35%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, CTCAE (3.0)

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 after the first publication or presentation that involves the overall study. Sponsor may request that confidential information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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