ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: October 11, 2016

ClinicalTrials.gov ID: NCT00412217

Study Identification

Unique Protocol ID:	ML20294
Brief Title:	A Study of Erlotinib (Tarceva) in Participants With Resected Head and Neck Squamous Cell Cancer
Official Title:	Phase III Randomized, Controlled Trial of Erlotinib (Tarceva) as Maintenance Therapy in Patients With Squamous Cell Carcinoma of the Head and Neck Treated With Resection and Radiotherapy With or Without Concomitant Chemotherapy With Curative Aim
Secondary IDs:	2006-001845-33 [EudraCT Number]

Study Status

Record Verification:	October 2016
Overall Status:	Terminated [The study was terminated because recruitment was too slow.]
Study Start:	November 2006
Primary Completion:	December 2009 [Actual]
Study Completion:	December 2009 [Actual]

Sponsor/Collaborators

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

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: Unknown Board Name: Comite Etico de Investigacion Clinica del Hospital Clinic i Provincial de Barcelona Board Affiliation: Unknown Phone: +34 93 227 57 86 Email: xcarne@clinic.ub.es
Data Monitoring?:	
Plan to Share IPD?:	
Oversight Authorities:	Spain: Ministry of Health

Study Description

Brief Summary:	This two-arm study will compare the efficacy and safety of erlotinib (Tarceva) versus placebo in participants with resected head and neck squamous cell cancer who are receiving concurrent chemoradiotherapy or radiotherapy alone. Participants will be randomized to receive either erlotinib 150 milligrams (mg) orally (PO) once daily or placebo for 1 year until disease progression or unacceptable toxicity.
Detailed Description:	

Conditions

Conditions:	Head and Neck Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 94 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Erlotinib Participants treated with surgical resection and chemoradiotherapy or radiotherapy alone will receive erlotinib tablets as 150 mg PO daily for 1 year until disease progression or intolerable toxicity.	Drug: Erlotinib Erlotinib will be given as 150 mg PO once daily. Other Names: • Tarceva Standard of care Additional clinical management including surgical resection and chemoradiotherapy or radiotherapy alone will be at the discretion of the Investigator according to local standard of care.
Placebo Comparator: Placebo Participants treated with surgical resection and chemoradiotherapy or radiotherapy alone will receive placebo treatment for 1 year until disease progression or intolerable toxicity.	Drug: Placebo Participants will receive placebo tablets (matched to erlotinib) once daily. Standard of care Additional clinical management including surgical resection and chemoradiotherapy or radiotherapy alone will be at the discretion of the Investigator according to local standard of care.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Adults greater than or equal to (≥) 18 years of age
- Curatively treated head and neck squamous cell cancer with T3-T4 and/or N2-N3 pathology, with or without other findings of poor prognosis such as extranodal extension, positive resection margins, and perineural or vascular involvement
- Eastern Cooperative Oncology Group (ECOG) status of 0 to 2

Exclusion Criteria:

- Macroscopic residual disease after surgery
- Previous treatment with anti-epidermal growth factor receptor (anti-EGFR) targeted therapies

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Spain

Salamanca, Spain, 37007

Santander, Spain, 39008

Valencia, Spain, 46015

Barcelona, Spain, 08907

Burgos, Spain, 09005

Barcelona, Spain, 08036

San Sebastian, Spain, 20012

Valencia, Spain, 41014

Valencia, Spain, 46026

Zaragoza, Spain, 50009

Alcorcon, Spain, 28922

Madrid, Spain, 28040

Madrid, Spain, 28041

Madrid, Spain, 28006

Granada, Spain, 18014

Sevilla, Spain, 41013

Sevilla, Spain, 41009

Cordoba, Spain, 14004

Madrid, Spain, 28033

Murcia, Spain, 30008

Lugo, Spain, 27004

San Sebastian, Spain, 20080

Palma de Mallorca, Spain, 07014

Madrid, Spain, 28007

Zamora, Spain, 49021

Jaen, Spain, 23007

Madrid, Spain, 28040

Guadalajara, Spain, 19002

Toledo, Spain, 45004

Orense, Spain, 32005

Barcelona, Spain, 08916

Barcelona, Spain, 08025

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Erlotinib	Participants with histologically confirmed advanced squamous cell carcinoma (SCC) of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received erlotinib tablets as 150 milligrams (mg) once daily for 1 year until disease progression or intolerable toxicity.
Placebo	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received placebo tablets (matched to erlotinib) once daily for 1 year until disease progression or intolerable toxicity.

Overall Study

	Erlotinib	Placebo
Started	46	48
Completed	0	0
Not Completed	46	48
Insufficient Data Available	8	3
Death	5	4
Disease Progression	2	3
Investigator Decision	1	0
Withdrawal by Subject	2	0
Lost to Follow-up	1	4
Study Terminated by Sponsor	26	33
Not Specified	1	1

Baseline Characteristics

Baseline Analysis Population Description

Intent-to-Treat (ITT) Population: All participants who were randomized in the study.

Reporting Groups

	Description
Erlotinib	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received erlotinib tablets as 150 mg once daily for 1 year until disease progression or intolerable toxicity.
Placebo	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received placebo tablets (matched to erlotinib) once daily for 1 year until disease progression or intolerable toxicity.

Baseline Measures

		Erlotinib	Placebo	Total
Overall Number of Participants		46	48	94
Age, Customized Measure Type: Number Unit of measure: participants	Number Analyzed	46 participants	48 participants	94 participants
18 Years or Older		46	48	94
Gender, Customized Measure Type: Number Unit of measure: participants	Number Analyzed	46 participants	48 participants	94 participants
Female		3	7	10
Male		42	41	83
Unknown		1	0	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With Disease Progression

Measure Description	Tumor response was assessed by the Investigator according to standard-of-care criteria, as there were no protocol-specified criteria for the assessment of tumor response and the instrument for assessment was deferred to the Investigator. To ensure comparability, baseline radiological studies later used to verify progression must be performed using identical techniques. The number of participants who experienced disease progression was reported.
Time Frame	From inclusion in the study until disease progression (maximum up to 3 years overall)
Safety Issue?	No

Analysis Population Description

ITT Population.

Reporting Groups

	Description
Erlotinib	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received erlotinib tablets as 150 mg once daily for 1 year until disease progression or intolerable toxicity.
Placebo	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received placebo tablets (matched to erlotinib) once daily for 1 year until disease progression or intolerable toxicity.

Measured Values

	Erlotinib	Placebo
Number of Participants Analyzed	46	48
Number of Participants With Disease Progression Measure Type: Number Unit of measure: participants	15	11

2. Primary Outcome Measure:

Measure Title	Time to Progression (TTP)
Measure Description	Tumor response was assessed by the Investigator according to standard-of-care criteria, as there were no protocol-specified criteria for the assessment of tumor response and the instrument for assessment was deferred to the Investigator. TTP was defined as the time from inclusion in the study to the time of disease progression, appearance of second tumor, or death from any cause, whichever occurred first. To ensure comparability, baseline radiological studies later used to verify progression must be performed using identical techniques. The median duration of TTP and corresponding 95% confidence interval (CI) were to be estimated by Kaplan-Meier analysis and expressed in months.
Time Frame	From inclusion in the study until disease progression, appearance of second tumor, or death from any cause (maximum up to 3 years overall)

Safety Issue?	No

Analysis Population Description
ITT Population.

Reporting Groups

	Description
Erlotinib	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received erlotinib tablets as 150 mg once daily for 1 year until disease progression or intolerable toxicity.
Placebo	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received placebo tablets (matched to erlotinib) once daily for 1 year until disease progression or intolerable toxicity.

Measured Values

	Erlotinib	Placebo
Number of Participants Analyzed	46	48
Time to Progression (TTP) Median (95% Confidence Interval) Unit of measure: months	NA (13.6259 to NA) [1]	NA (18.4110 to NA) [1]

[1] The median and upper limit of the 95% CI for PFS were not reached during the study period and could not be calculated.

3. Secondary Outcome Measure:

Measure Title	Number of Participants Who Died
Measure Description	The number of participants who died from any cause was reported.
Time Frame	From inclusion in the study until death from any cause (maximum up to 3 years overall)
Safety Issue?	No

Analysis Population Description
ITT Population.

Reporting Groups

	Description
Erlotinib	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received erlotinib tablets as 150 mg once daily for 1 year until disease progression or intolerable toxicity.
Placebo	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received placebo tablets (matched to erlotinib) once daily for 1 year until disease progression or intolerable toxicity.

Measured Values

	Erlotinib	Placebo
Number of Participants Analyzed	46	48
Number of Participants Who Died Measure Type: Number Unit of measure: participants	7	5

4. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	OS was defined as the time from inclusion in the study to date of death for any reason. The median duration of OS and corresponding 95% CI were to be estimated by Kaplan-Meier analysis and expressed in months.
Time Frame	From inclusion in the study until death from any cause (maximum up to 3 years overall)
Safety Issue?	No

Analysis Population Description

ITT Population.

Reporting Groups

	Description
Erlotinib	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received erlotinib tablets as 150 mg once daily for 1 year until disease progression or intolerable toxicity.
Placebo	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received placebo tablets (matched to erlotinib) once daily for 1 year until disease progression or intolerable toxicity.

Measured Values

	Erlotinib	Placebo
Number of Participants Analyzed	46	48
Overall Survival (OS) Median (95% Confidence Interval) Unit of measure: months	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] The lower limit of the 95% CI for OS was not reached during the study period and therefore no values could be calculated.

Reported Adverse Events

Time Frame	From Baseline until end of treatment (up to 1 year)
Additional Description	ITT Population. Adverse events (AEs) are organized by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC), but the AE terms included below are same as they were originally registered and saved.

Reporting Groups

	Description
Erlotinib	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received erlotinib tablets as 150 mg once daily for 1 year until disease progression or intolerable toxicity.
Placebo	Participants with histologically confirmed advanced SCC of the head and neck, treated with surgical resection and chemoradiotherapy or radiotherapy alone, received placebo tablets (matched to erlotinib) once daily for 1 year until disease progression or intolerable toxicity.

Serious Adverse Events

	Erlotinib	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	4/46 (8.7%)	2/48 (4.17%)
Blood and lymphatic system disorders		
Anemia [A] *	1/46 (2.17%)	0/48 (0%)
Gastrointestinal disorders		

	Erlotinib	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Dysphagia [A] *	1/46 (2.17%)	0/48 (0%)
Infections and infestations		
Pneumonia [A] *	0/46 (0%)	1/48 (2.08%)
Respiratory tract infection [A] *	1/46 (2.17%)	0/48 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Resection of right cervical tumor [A] *	0/46 (0%)	1/48 (2.08%)
Surgical and medical procedures		
Dental extraction [A] *	1/46 (2.17%)	0/48 (0%)
Vascular disorders		
Aneurism [A] *	1/46 (2.17%)	0/48 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.1)

Other Adverse Events

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

	Erlotinib	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Total	36/46 (78.26%)	31/48 (64.58%)
Blood and lymphatic system disorders		
Anemia [A] *	2/46 (4.35%)	4/48 (8.33%)
Ear and labyrinth disorders		
Acufenos [A] *	2/46 (4.35%)	3/48 (6.25%)
Earache [A] *	4/46 (8.7%)	2/48 (4.17%)
Gastrointestinal disorders		
Diarrhea [A] *	12/46 (26.09%)	0/48 (0%)
Dry mouth [A] *	12/46 (26.09%)	18/48 (37.5%)

	Erlotinib	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Dyspesia [A] *	3/46 (6.52%)	2/48 (4.17%)
Dysphagia [A] *	6/46 (13.04%)	7/48 (14.58%)
Odynophagia [A] *	1/46 (2.17%)	9/48 (18.75%)
Stomatitus [A] *	2/46 (4.35%)	3/48 (6.25%)
General disorders		
Asthenia [A] *	15/46 (32.61%)	11/48 (22.92%)
Edema [A] *	3/46 (6.52%)	5/48 (10.42%)
Localized edema [A] *	4/46 (8.7%)	4/48 (8.33%)
Mucosa inflammation [A] *	7/46 (15.22%)	5/48 (10.42%)
Pyrexia [A] *	5/46 (10.87%)	0/48 (0%)
Infections and infestations		
Folliculitis [A] *	7/46 (15.22%)	1/48 (2.08%)
Metabolism and nutrition disorders		
Anorexia [A] *	5/46 (10.87%)	7/48 (14.58%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	4/46 (8.7%)	4/48 (8.33%)
Musculoskeletal pain [A] *	5/46 (10.87%)	3/48 (6.25%)
Musculoskeletal rigidity [A] *	3/46 (6.52%)	3/48 (6.25%)
Neck pain [A] *	5/46 (10.87%)	5/48 (10.42%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	4/46 (8.7%)	5/48 (10.42%)
Dyspnea [A] *	2/46 (4.35%)	4/48 (8.33%)
Skin and subcutaneous tissue disorders		

	Erlotinib	Placebo
	Affected/At Risk (%)	Affected/At Risk (%)
Acne [A] *	6/46 (13.04%)	0/48 (0%)
Dermatitis [A] *	7/46 (15.22%)	1/48 (2.08%)
Rash [A] *	8/46 (17.39%)	1/48 (2.08%)
Skin toxicity [A] *	5/46 (10.87%)	0/48 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.1)

Limitations and Caveats

The Study was terminated early as a result of slow recruitment. Results should be interpreted with consideration of the small sample size.

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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