ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/14/2016

ClinicalTrials.gov ID: NCT00642473

Study Identification

Unique Protocol ID:	ML21308
Brief Title:	A Study of Metronidazole Cream in the Prevention and Treatment of Tarceva (Erlotinib)-Associated Rash (MATER)
Official Title:	A Phase II Trial Assessing Metronidazol Actavis 1% Topical Cream in the Prevention and Treatment of Erlotinib Associated Rash
Secondary IDs:	2007-002895-32 [EudraCT Number]

Study Status

Record Verification:	April 2016
Overall Status:	Completed
Study Start:	February 2008
Primary Completion:	March 2009 [Actual]
Study Completion:	March 2009 [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: 333/207 Board Name: Regional Ethics Committee Board Affiliation: Lund Phone: 46462224180 Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Sweden: Central Ethics Committee, Stockholm

Study Description

Brief Summary:	This study will evaluate the efficacy and safety of metronidazole actavis 1 percent (%) topical cream in the prevention and treatment of rash associated with Tarceva treatment, in participants with non-small cell lung cancer. The first cohort of participants enrolled in the study will be treated twice daily with metronidazole cream on the right side of the face and upper thorax, the same day as they start treatment with Tarceva (150 mg orally daily). The corresponding body parts on the left side will be treated according to local standard procedures (ie, with non-active moisturizing cream). The second cohort of Tarceva-treated participants will only receive twice daily treatment with metronidazole cream if and when they develop rash. In both cohorts, efficacy will be evaluated at Week 2 and Week 4. The anticipated time on metronidazole treatment is less than (<) 3 months, and the target sample size is <100 individuals.
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:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Non-Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 34 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Prevention (Erlotinib + Metronidazole Actavis) Participants will receive erlotinib orally daily. Metronidazole actavis treatment will be initiated at the same day as the start of erlotinib. Metronidazole actavis 1% topical cream will be applied on the right side of the face and chest twice daily for 4 weeks. Left side of the face and chest will be treated according to local standard procedures (ie, with non-active moisturizing cream).	Drug: Erlotinib Participants will receive erlotinib 150 milligrams (mg) orally daily for 4 weeks. Other Names: • Tarceva Drug: Metronidazole Actavis Metronidazole actavis 1% topical cream will be applied on the face and chest twice daily for 4 weeks. Non-active Moisturizing Cream Left side of the face and chest will be treated according to local standard procedures (ie, with non-active moisturizing cream).
Experimental: Treatment (Erlotinib + Metronidazole Actavis) Participants will receive erlotinib orally daily. Metronidazole actavis treatment will be initiated when participants develop rash. Metronidazole actavis 1% topical cream will be applied on the right side of the face and chest twice daily for 4 weeks. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream).	Drug: Erlotinib Participants will receive erlotinib 150 milligrams (mg) orally daily for 4 weeks. Other Names: • Tarceva Drug: Metronidazole Actavis Metronidazole actavis 1% topical cream will be applied on the face and chest twice daily for 4 weeks. Non-active Moisturizing Cream Left side of the face and chest will be treated according to local standard procedures (ie, with non-active moisturizing cream).

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- non-small cell lung cancer
- eligible to start treatment with erlotinib

Exclusion Criteria:

- hypersensitivity to metronidazole

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Sweden
Malmoe, Sweden, 20502

Goeteborg, Sweden, 41345

Lund, Sweden, 22185

Stockholm, Sweden, S-14186

Umea, Sweden, S-901 85

Vaxjo, Sweden, 35185

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Prevention (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 milligrams (mg) orally daily. Metronidazole actavis treatment was initiated the same day as the start of erlotinib. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the prevention of erlotinib associated rash. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream).
Treatment (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated when participants developed rash. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the treatment of erlotinib associated rash. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream).

Overall Study

	Prevention (Erlotinib + Metronidazole Actavis)	Treatment (Erlotinib + Metronidazole Actavis)
Started	18	16
Completed	14	5
Not Completed	4	11
Withdrawal by Subject	0	5
Progression or death	2	4
Unspecified	2	2

Baseline Characteristics

Analysis Population Description

All enrolled participants

Reporting Groups

	Description
Prevention (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated the same day as the start of erlotinib. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the prevention of erlotinib associated rash. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream).
Treatment (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated when participants developed rash. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the treatment of erlotinib associated rash. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream).

Baseline Measures

	Prevention (Erlotinib + Metronidazole Actavis)	Treatment (Erlotinib + Metronidazole Actavis)	Total
Number of Participants	18	16	34
Age, Continuous [units: years] Mean (Standard Deviation)	68 (10.8)	70 (13.1)	69 (11.8)
Gender, Male/Female [units: participants]			
Female	11	12	23
Male	7	4	11

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Erlotinib Associated Rash Stratified by Severity Grade at Week 2
Measure Description	Severity of the rash was evaluated semi-quantitatively using the scale of Common Terminology Criteria for Adverse Events version 3.0 (CTCAE v3.0). Grade 0: no rash; Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe; Grade 4: Life-threatening or disabling; Grade 5: Death related to rash. Same participant may be counted in more than one reported categories.
Time Frame	After 2 weeks of metronidazole treatment
Safety Issue?	No

Analysis Population Description

All enrolled participants. Here, number of participants analyzed = participants who were evaluable for this outcome in respective arms.

Reporting Groups

	Description
Left Side - Prevention (Erlotinib + Standard Procedures)	Participants received erlotinib 150 mg orally daily for 4 weeks. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream) to evaluate whether it was effective in the prevention of erlotinib associated rash .
Right Side - Prevention (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated when participants developed rash. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the prevention of erlotinib associated rash.
Left Side - Treatment (Erlotinib + Standard Procedures)	Participants received erlotinib 150 mg orally daily for 4 weeks. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream) to evaluate whether it was effective in the treatment of erlotinib associated rash.
Right Side - Treatment (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated when participants developed rash. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the treatment of erlotinib associated rash.

Measured Values

	Left Side - Prevention (Erlotinib + Standard Procedures)	Right Side - Prevention (Erlotinib + Metronidazole Actavis)	Left Side - Treatment (Erlotinib + Standard Procedures)	Right Side - Treatment (Erlotinib + Metronidazole Actavis)
Number of Participants Analyzed	9	9	6	6
Percentage of Participants With Erlotinib Associated Rash Stratified by Severity Grade at Week 2 [units: percentage of participants]				
Facial Rash: Grade 0 (n=9,9,6,6)	11	22	0	33
Chest Rash: Grade 0 (n=9,9,6,6)	56	56	33	50
Facial Rash: Grade 1 (n=9,9,6,6)	33	22	50	33
Chest Rash: Grade 1 (n=9,9,6,6)	33	33	17	17
Facial Rash: Grade 2 (n=9,9,6,6)	22	33	33	17
Chest Rash: Grade 2 (n=9,9,6,6)	11	11	33	17
Facial Rash: Grade 3 (n=9,9,6,6)	33	22	17	17
Chest Rash: Grade 3 (n=9,9,6,6)	0	0	17	17

	Left Side - Prevention (Erlotinib + Standard Procedures)	Right Side - Prevention (Erlotinib + Metronidazole Actavis)	Left Side - Treatment (Erlotinib + Standard Procedures)	Right Side - Treatment (Erlotinib + Metronidazole Actavis)
Facial Rash: Grade 4 (n=9,9,6,6)	0	0	0	0
Chest Rash: Grade 4 (n=9,9,6,6)	0	0	0	0
Facial Rash: Grade 5 (n=9,9,6,6)	0	0	0	0
Chest Rash: Grade 5 (n=9,9,6,6)	0	0	0	0

2. Primary Outcome Measure:

Measure Title	Percentage of Participants With Erlotinib Associated Rash Stratified by Severity Grade at Week 4
Measure Description	Severity of the rash was evaluated semi-quantitatively using the scale of CTCAE v3.0. Grade 0: no rash; Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe; Grade 4: Life-threatening or disabling; Grade 5: Death related to rash. Same participant may be counted in more than one reported categories.
Time Frame	After 4 weeks of metronidazole treatment
Safety Issue?	No

Analysis Population Description

All enrolled participants. Here, number of participants analyzed = participants who were evaluable for this outcome in respective arms.

Reporting Groups

	Description
Left Side - Prevention (Erlotinib + Standard Procedures)	Participants received erlotinib 150 mg orally daily for 4 weeks. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream) to evaluate whether it was effective in the prevention of erlotinib associated rash.
Right Side - Prevention (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated when participants developed rash. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the prevention of erlotinib associated rash.
Left Side - Treatment (Erlotinib + Standard Procedures)	Participants received erlotinib 150 mg orally daily for 4 weeks. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream) to evaluate whether it was effective in the treatment of erlotinib associated rash.

	Description
Right Side - Treatment (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated when participants developed rash. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the treatment of erlotinib associated rash.

Measured Values

	Left Side - Prevention (Erlotinib + Standard Procedures)	Right Side - Prevention (Erlotinib + Metronidazole Actavis)	Left Side - Treatment (Erlotinib + Standard Procedures)	Right Side - Treatment (Erlotinib + Metronidazole Actavis)
Number of Participants Analyzed	8	8	4	4
Percentage of Participants With Erlotinib Associated Rash Stratified by Severity Grade at Week 4 [units: percentage of participants]				
Facial Rash: Grade 0 (n=8,8,4,4)	13	25	0	25
Chest Rash: Grade 0 (n=8,8,4,4)	75	63	25	50
Facial Rash: Grade 1 (n=8,8,4,4)	63	50	50	50
Chest Rash: Grade 1 (n=8,8,4,4)	0	13	25	25
Facial Rash: Grade 2 (n=8,8,4,4)	13	25	25	50
Chest Rash: Grade 2 (n=8,8,4,4)	13	13	25	25
Facial Rash: Grade 3 (n=8,8,4,4)	0	0	0	0
Chest Rash: Grade 3 (n=8,8,4,4)	0	13	0	0
Facial Rash: Grade 4 (n=8,8,4,4)	13	0	0	0
Chest Rash: Grade 4 (n=8,8,4,4)	13	0	0	0
Facial Rash: Grade 5 (n=8,8,4,4)	0	0	0	0
Chest Rash: Grade 5 (n=8,8,4,4)	0	0	0	0

Reported Adverse Events

Time Frame	Baseline to Week 4
Additional Description	Adverse events were not coded using MedDRA or any other standard coding dictionary. Rash was considered an efficacy parameter only and was not considered an adverse event for this study.

Reporting Groups

	Description
Prevention (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated the same day as the start of erlotinib. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the prevention of erlotinib associated rash. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream).
Treatment (Erlotinib + Metronidazole Actavis)	Participants received erlotinib 150 mg orally daily. Metronidazole actavis treatment was initiated when participants developed rash. Metronidazole actavis 1% topical cream was applied on the right side of the face and chest twice daily for 4 weeks to evaluate whether it was effective in the treatment of erlotinib associated rash. Left side of the face and chest was treated according to local standard procedures (ie, with non-active moisturizing cream).

Serious Adverse Events

	Prevention (Erlotinib + Metronidazole Actavis)	Treatment (Erlotinib + Metronidazole Actavis)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	3/18 (16.67%)	5/16 (31.25%)
Gastrointestinal disorders		
Diarrhea *	1/18 (5.56%)	0/16 (0%)
General disorders		
Falling *	0/18 (0%)	1/16 (6.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Death *	2/18 (11.11%)	3/16 (18.75%)
Respiratory, thoracic and mediastinal disorders		
Dyspnea *	0/18 (0%)	1/16 (6.25%)

* Indicates events were collected by non-systematic methods.

Other Adverse Events

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

	Prevention (Erlotinib + Metronidazole Actavis)	Treatment (Erlotinib + Metronidazole Actavis)
	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/18 (33.33%)	1/16 (6.25%)
Gastrointestinal disorders		
Aphthae *	1/18 (5.56%)	0/16 (0%)
Diarrhea *	4/18 (22.22%)	1/16 (6.25%)
Pain *	1/18 (5.56%)	0/16 (0%)

* Indicates events were collected by non-systematic methods.

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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