ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 09/14/2012

ClinicalTrials.gov ID: NCT00597116

Study Identification

Unique Protocol ID:	D4200C00075
Brief Title:	An Efficacy and Safety Study With Vandetanib to Treat Inoperable or Relapsed Malignant Mesothelioma
Official Title:	A Randomized Phase II Trial To Evaluate The Efficacy And Safety Of Vandetanib (ZD6474, ZACTIMA ™) Versus Vinorelbine In Patients With Inoperable Or Relapsed Malignant Mesothelioma.
Secondary IDs:	EUDRACT Number 2007-003633-16

Study Status

Record Verification:	September 2012
Overall Status:	Terminated
Study Start:	December 2007
Primary Completion:	January 2010 [Actual]
Study Completion:	January 2010 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
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: EK-1474 Board Name: KEK Zurich Board Affiliation: KEK Zurich Phone: 0041 43 269 52 11 Email: niklaus.herzog@gd.zh.ch
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Germany: Federal Institute for Drugs and Medical Devices Switzerland: Swissmedic

Study Description

Brief Summary:	A clinical study to assess if a new investigational drug is effective in treating malignant mesothelioma, compared to a chemotherapy treatment (Navelbine®). In this study the patients will be assigned by chance to receive either the new drug or a chemotherapy treatment (Navelbine®). Treatment will continue as long as the cancer does not worsen and the patient wishes to continue in the study. The study will recruit approximately 66 patients.
Detailed Description:	

Conditions

Conditions:	Mesothelioma
Keywords:	Mesothelioma inoperable relapsed

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:	Efficacy Study
Enrollment:	25 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: 1 Vinorelbine	Drug: Vinorelbine Other Names: • Navelbine®
Experimental: 2 Vandetanib	Drug: Vandetanib once daily oral dose Other Names: • ZD6474 • ZACTIMA™

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Diagnosed with mesothelioma
- Previously treated with only one course of chemotherapy for mesothelioma
- No previous treatment with vinorelbine
- No serious heart problems within the last 3 months

Exclusion Criteria:

- Serious abnormal laboratory values
- Severe or uncontrolled disease or condition as judged by the Investigator
- Pregnant or breast-feeding women

- Other cancers within the last 5 years
- Major surgery or radiation therapy within 4 weeks prior to starting study therapy
- Receipt of any investigational agents within 30 days prior to commencing study treatment.

Contacts/Locations

Study Officials:

Rolf Stahel
Study Principal Investigator
University Hospital of Zurich

Dirk Schneider
Study Director
AstraZeneca

Erica Pellicioli, PhD
Study Chair
AstraZeneca

Locations:

Germany
Research Site
Heidelberg, Germany

Research Site
Essen, Germany

Switzerland
Research Site
Zurich, Switzerland

Germany
Research Site
Hamburg, Germany

Research Site
Halle-Dolau, Germany

Switzerland
Research Site
Chur, Switzerland

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	First subject enrolled: 17 December 2007, Last subject last visit: 22 July 2009. The study was conducted at 2 centres in Switzerland and 4 centres in Germany.

Reporting Groups

	Description
Vandetanib	Vandetanib 300 mg/day oral
Vinorelbine	Vinorelbine 30 mg/m2 iv, administrated weekly

Overall Study

	Vandetanib	Vinorelbine
Started	14	11
Completed	0 [1]	0 [1]
Not Completed	14	11
Adverse Event	2	1
Withdrawal by Subject	0	2
Physician Decision	0	1
Death	0	1
Lost to Follow-up	1	0
Progressive disease	11	6

[1] Randomised patients ongoing study treatment at data cut-off

Baseline Characteristics

Reporting Groups

	Description
Vandetanib	Vandetanib 300 mg/day oral
Vinorelbine	Vinorelbine 30 mg/m2 iv, administrated weekly

Baseline Measures

	Vandetanib	Vinorelbine	Total
Number of Participants	13	10	23
Age, Continuous [units: Years] Median (Full Range)	67 (54 to 77)	64 (27 to 76)	65.5 (27 to 77)
Gender, Male/Female [units: Participants]			
Female	1	0	1
Male	12	10	22

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With Disease Control.
Measure Description	Disease control is defined as having a complete response (CR), a partial response (PR) or stable disease (SD) according to the modified RECIST criteria for assessment of response in malignant pleural mesothelioma. CR is defined as the disappearance of all target lesions with no evidence of tumour elsewhere and PR is defined as at least a 30% reduction in the total tumour measurement. A confirmed response requires a repeat observation on two occasions 4 weeks apart. PD is defined as an increase of at least 20% in the total tumour measurement over the nadir measurement, or the appearance of one or more new lesions. Patients with SD are those who fulfill the criteria for neither PR nor PD.
Time Frame	Assessed at 2 months.
Safety Issue?	No

Analysis Population Description

Only patients in the evaluable for efficacy population were included.It was defined as all treated patients with no major deviations from the eligibility criteria affecting the evaluation of efficacy, who completed at least 2 cycles(unless progressive disease occurred at cycle 1)and who had at least one post-treatment tumour assessment.

Reporting Groups

	Description
Vandetanib	Vandetanib 300 mg/day oral
Vinorelbine	Vinorelbine 30 mg/m2 iv, administrated weekly

Measured Values

	Vandetanib	Vinorelbine
Number of Participants Analyzed	12	10
Number of Participants With Disease Control. [units: Participants]	0	5

2. Secondary Outcome Measure:

Measure Title	Number of Participants With Objective Response.
Measure Description	Objective response is defined as having a complete response (CR) or a partial response (PR) according to the modified RECIST criteria for assessment of response in malignant pleural mesothelioma. CR is defined as the disappearance of all target lesions with no evidence of tumour elsewhere and PR is defined as at least a 30% reduction in the total tumour measurement. A confirmed response requires a repeat observation on two occasions 4 weeks apart.
Time Frame	Assessed at 2 months.
Safety Issue?	No

Analysis Population Description

Only patients in the evaluable for efficacy population were included. It was defined as all treated patients with no major deviations from the eligibility criteria affecting the evaluation of efficacy, who completed at least 2 cycles (unless progressive disease occurred at cycle 1) and who had at least one post-treatment tumour assessment.

Reporting Groups

	Description
Vandetanib	Vandetanib 300 mg/day oral
Vinorelbine	Vinorelbine 30 mg/m2 iv, administrated weekly

Measured Values

	Vandetanib	Vinorelbine
Number of Participants Analyzed	12	10
Number of Participants With Objective Response.	0	0

	Vandetanib	Vinorelbine
[units: Participants]		

3. Secondary Outcome Measure:

Measure Title	Progression-free Survival (PFS)
Measure Description	Time from randomization to date of documented response of progressive disease (PD) as assessed according to the modified RECIST criteria for assessment of response in malignant pleural mesothelioma. PD is defined as an increase of at least 20% in the total tumour measurement over the nadir measurement, or the appearance of one or more new lesions.
Time Frame	Assessed from baseline to 12 months.
Safety Issue?	No

Analysis Population Description

Only patients in the evaluable for efficacy population were included. It was defined as all treated patients with no major deviations from the eligibility criteria affecting the evaluation of efficacy, who completed at least 2 cycles (unless progressive disease occurred at cycle 1) and who had at least one post-treatment tumour assessment.

Reporting Groups

	Description
Vandetanib	Vandetanib 300 mg/day oral
Vinorelbine	Vinorelbine 30 mg/m2 iv, administrated weekly

Measured Values

	Vandetanib	Vinorelbine
Number of Participants Analyzed	12	10
Progression-free Survival (PFS) [units: Months] Median (95% Confidence Interval)	1.8 (1.1 to 1.8)	3.8 (2.1 to 7.3)

4. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	

Time Frame	Assessed from baseline to 12 months.
Safety Issue?	No

Analysis Population Description

Only patients in the evaluable for efficacy population were included. It was defined as all treated patients with no major deviations from the eligibility criteria affecting the evaluation of efficacy, who completed at least 2 cycles (unless progressive disease occurred at cycle 1) and who had at least one post-treatment tumour assessment.

Reporting Groups

	Description
Vandetanib	Vandetanib 300 mg/day oral
Vinorelbine	Vinorelbine 30 mg/m2 iv, administrated weekly

Measured Values

	Vandetanib	Vinorelbine
Number of Participants Analyzed	12	10
Overall Survival (OS) [units: Months] Median (95% Confidence Interval)	7.8 (2.5 to 12.5)	6.4 (3.6 to 14.9)

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	The enrolled and randomised population was Vandetanib 14 & Vinorelbine 11. However, demographic and baseline characteristics were analyzed for evaluable patients = safety population (Vandetanib 13 & Vinorelbine 10)

Reporting Groups

	Description
Vandetanib	Vandetanib 300 mg/day oral
Vinorelbine	Vinorelbine 30 mg/m2 iv, administrated weekly

Serious Adverse Events

	Vandetanib	Vinorelbine
	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/13 (46.15%)	3/10 (30%)
Blood and lymphatic system disorders		
Febrile Neutropoenia [A] *	2/13 (15.38%)	0/10 (0%)
Cardiac disorders		
Angina Pectoris [A] *	0/13 (0%)	1/10 (10%)
Gastrointestinal disorders		
Acute Abdomen [A] *	1/13 (7.69%)	0/10 (0%)
Gastrointestinal Haemorrhage [A] *	1/13 (7.69%)	0/10 (0%)
Inguinal Hernia [A] *	1/13 (7.69%)	0/10 (0%)
General disorders		
Deterioration Of General Health [A] *	1/13 (7.69%)	0/10 (0%)
Pyrexia [A] *	1/13 (7.69%)	0/10 (0%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [A] *	1/13 (7.69%)	1/10 (10%)
Vascular disorders		
Papilloedema [A] *	0/13 (0%)	1/10 (10%)
Pulmonary Embolism [A] *	0/13 (0%)	1/10 (10%)
Venous stasis [A] *	1/13 (7.69%)	0/10 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 10.0

Other Adverse Events

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

	Vandetanib	Vinorelbine
	Affected/At Risk (%)	Affected/At Risk (%)
Total	13/13 (100%)	10/10 (100%)
Blood and lymphatic system disorders		
Anaemia [A] †	0/13 (0%)	3/10 (30%)
Febrile Neutropenia [A] †	0/13 (0%)	1/10 (10%)
Ear and labyrinth disorders		
Ear Discomfort [A] †	0/13 (0%)	1/10 (10%)
Vertigo [A] †	0/13 (0%)	2/10 (20%)
Endocrine disorders		
Hypothyroidism [A] †	0/13 (0%)	1/10 (10%)
Gastrointestinal disorders		
Abdominal Distension [A] †	1/13 (7.69%)	0/10 (0%)
Abdominal Pain [A] †	2/13 (15.38%)	1/10 (10%)
Abdominal Pain Upper [A] †	0/13 (0%)	3/10 (30%)
Anal Haemorrhage [A] †	1/13 (7.69%)	0/10 (0%)
Cheilitis [A] †	0/13 (0%)	1/10 (10%)
Constipation [A] †	3/13 (23.08%)	3/10 (30%)
Diarrhoea [A] †	3/13 (23.08%)	1/10 (10%)
Dyspepsia [A] †	0/13 (0%)	1/10 (10%)
Flatulence [A] †	2/13 (15.38%)	0/10 (0%)
Nausea [A] †	4/13 (30.77%)	6/10 (60%)
Oral Pain [A] †	0/13 (0%)	1/10 (10%)
Rectal Haemorrhage [A] †	0/13 (0%)	1/10 (10%)

	Vandetanib	Vinorelbine
	Affected/At Risk (%)	Affected/At Risk (%)
Vomiting [A] †	0/13 (0%)	1/10 (10%)
General disorders		
Asthenia [A] †	1/13 (7.69%)	1/10 (10%)
Chest Pain [A] †	0/13 (0%)	3/10 (30%)
Fatigue [A] †	5/13 (38.46%)	6/10 (60%)
General Physical Health Deterioration [A] †	2/13 (15.38%)	0/10 (0%)
Mucosal Inflammation [A] †	0/13 (0%)	1/10 (10%)
Oedema [A] †	1/13 (7.69%)	0/10 (0%)
Oedema Peripheral [A] †	1/13 (7.69%)	1/10 (10%)
Orthostatic Intolerance [A] †	0/13 (0%)	1/10 (10%)
Pain [A] †	0/13 (0%)	1/10 (10%)
Pyrexia [A] †	1/13 (7.69%)	1/10 (10%)
Infections and infestations		
Blood Alkaline Phosphatase Increased [A] †	0/13 (0%)	1/10 (10%)
Bronchitis [A] †	0/13 (0%)	1/10 (10%)
Gastrointestinal Infection [A] †	0/13 (0%)	1/10 (10%)
Infection [A] †	1/13 (7.69%)	0/10 (0%)
Influenza [A] †	1/13 (7.69%)	0/10 (0%)
Liver Function Test Abnormal [A] †	1/13 (7.69%)	0/10 (0%)
Nasopharyngitis [A] †	1/13 (7.69%)	3/10 (30%)
Neutrophil Count Decreased [A] †	0/13 (0%)	8/10 (80%)
Pneumonia [A] †	0/13 (0%)	1/10 (10%)

	Vandetanib	Vinorelbine
	Affected/At Risk (%)	Affected/At Risk (%)
Rhinitis [A] †	2/13 (15.38%)	0/10 (0%)
Urinary Tract Infection [A] †	0/13 (0%)	1/10 (10%)
Weight Decreased [A] †	2/13 (15.38%)	3/10 (30%)
White Blood Cell Count Decreased [A] †	0/13 (0%)	2/10 (20%)
Metabolism and nutrition disorders		
Anorexia [A] †	7/13 (53.85%)	4/10 (40%)
Diabetes Mellitus Insulin-Dependent [A] †	0/13 (0%)	1/10 (10%)
Hypokalaemia [A] †	1/13 (7.69%)	0/10 (0%)
Musculoskeletal and connective tissue disorders		
Back Pain [A] †	0/13 (0%)	1/10 (10%)
Musculoskeletal Pain [A] †	1/13 (7.69%)	0/10 (0%)
Pain In Extremity [A] †	0/13 (0%)	1/10 (10%)
Pain In Jaw [A] †	0/13 (0%)	1/10 (10%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Tumour Pain [A] †	1/13 (7.69%)	0/10 (0%)
Nervous system disorders		
Dizziness [A] †	1/13 (7.69%)	1/10 (10%)
Dysgeusia [A] †	0/13 (0%)	1/10 (10%)
Neuropathy [A] †	0/13 (0%)	1/10 (10%)
Paraesthesia [A] †	0/13 (0%)	4/10 (40%)
Psychiatric disorders		
Depression [A] †	1/13 (7.69%)	0/10 (0%)
Mental Disorder [A] †	1/13 (7.69%)	0/10 (0%)

	Vandetanib	Vinorelbine
	Affected/At Risk (%)	Affected/At Risk (%)
Sleep Disorder [A] †	1/13 (7.69%)	0/10 (0%)
Renal and urinary disorders		
Nocturia [A] †	1/13 (7.69%)	0/10 (0%)
Oliguria [A] †	1/13 (7.69%)	0/10 (0%)
Reproductive system and breast disorders		
Benign Prostatic Hyperplasia [A] †	1/13 (7.69%)	0/10 (0%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	2/13 (15.38%)	1/10 (10%)
Dysphonia [A] †	1/13 (7.69%)	0/10 (0%)
Dyspnoea [A] †	3/13 (23.08%)	2/10 (20%)
Epistaxis [A] †	1/13 (7.69%)	0/10 (0%)
Hiccups [A] †	1/13 (7.69%)	0/10 (0%)
Skin and subcutaneous tissue disorders		
Acne [A] †	1/13 (7.69%)	0/10 (0%)
Alopecia [A] †	0/13 (0%)	1/10 (10%)
Dermatitis [A] †	1/13 (7.69%)	0/10 (0%)
Hyperhidrosis [A] †	1/13 (7.69%)	0/10 (0%)
Night Sweats [A] †	1/13 (7.69%)	0/10 (0%)
Pruritus [A] †	1/13 (7.69%)	0/10 (0%)
Rash [A] †	6/13 (46.15%)	0/10 (0%)
Urticaria [A] †	1/13 (7.69%)	0/10 (0%)
Vascular disorders		
Haematoma [A] †	1/13 (7.69%)	0/10 (0%)

	Vandetanib	Vinorelbine
	Affected/At Risk (%)	Affected/At Risk (%)
Hot Flush [A] †	1/13 (7.69%)	0/10 (0%)
Hypertension [A] †	1/13 (7.69%)	0/10 (0%)
Phlebitis [A] †	0/13 (0%)	1/10 (10%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.0

Limitations and Caveats

Early termination leading to small number of subjects analyzed.

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.

AstraZeneca shall have a period of 30 days from receipt of the proposed final manuscript for any publication or other disclosure to review it and may within such time require that submission for publication or disclosure of the manuscript be delayed for maximally six (6) months in order for AstraZeneca to file patent applications.

Results Point of Contact:

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