ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 04/27/2011

ClinicalTrials.gov ID: NCT00454116

Study Identification

Unique Protocol ID:	D4200C00048
Brief Title:	A Phase II, Double Blind Study of 2 Doses of ZACTIMA™(ZD6474) in Combination With FOLFIRI vs FOLFIRI Alone for the Treatment of Colorectal Cancer in Patients
Official Title:	A Phase II, Double Blind, Placebo Controlled, Randomised Study to Assess the Efficacy and Safety of 2 Doses of ZACTIMA™(ZD6474) in Combination With FOLFIRI vs FOLFIRI Alone for the Treatment of Colorectal Cancer in Patients Who Have Failed Therapy With Anoxaliplatin and Fluoropyrimidine Containing Regimen
Secondary IDs:	

Study Status

Record Verification:	April 2011
Overall Status:	Completed
Study Start:	March 2007
Primary Completion:	March 2008 [Actual]
Study Completion:	November 2009 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 60,042 Serial Number: 0463 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	The purpose of this study is to assess the efficacy and safety of 2 doses of ZACTIMA™ (ZD6474) in combination with FOLFIRI vs FOLFIRI alone for the treatment of colorectal cancer in patients who have failed therapy with an oxaliplatin and fluoropyrimidine containing regimen.
Detailed Description:	

Conditions

Conditions:	Colorectal Cancer
Keywords:	Colon Cancer Rectal Cancer

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment

Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	3
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	106 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Placebo Comparator: 1 FOLFIRI + placebo vandetanib	Drug: FOLFIRI Intravenous infusion
Experimental: 2 FOLFIRI + low dose vandetanib	Drug: Vandetanib once daily oral tablet two doses Other Names: • ZD6474 • ZACTIMA™ Drug: FOLFIRI Intravenous infusion
Experimental: 3 FOLFIRI + high dose vandetanib	Drug: Vandetanib once daily oral tablet two doses Other Names: • ZD6474 • ZACTIMA™ Drug: FOLFIRI Intravenous infusion

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Histologically confirmed colorectal cancer
- Have failed therapy with an oxaliplatin and fluoropyrimidine containing regimen defined as:
- Progression on or following treatment for metastatic colorectal cancer
- Progression within 12 months of adjuvant chemotherapy for colorectal cancer

Exclusion Criteria:

- Previous treatment with small molecule tyrosine kinase inhibitors of VEGFR or EGFR eg, erlotinib, gefitinib. Prior monoclonal antibodies are permitted, eg, cetuximab, bevacizumab.
- Previous adjuvant therapy with irinotecan within 12 months of randomization
- More than one prior course of chemotherapy for treatment of metastatic colorectal cancer.

Contacts/Locations

Study Officials: Zactima Medical Science Director, MD
Study Director
AstraZeneca

Locations: United States, Michigan
Research Site
Ann Arbor, Michigan, United States

United States, Tennessee
Research Site
Nashville, Tennessee, United States

United States, New York
Research Site
New York, New York, United States

Argentina
Research Site
Santa Fe, Argentina

Research Site
Buenos Aires, Argentina

Korea, Republic of
Research Site
Seoul, Korea, Republic of

Norway
Research Site
Oslo, Norway

Spain
Research Site
Barcelona, Spain

Research Site
Jaen, Spain

Research Site
Lleida, Spain

United Kingdom
Research Site
Manchester, United Kingdom

Research Site
Leicester, United Kingdom

Research site
Belfast, Northern Ireland, United Kingdom

Research Site
Aberdeen, United Kingdom

Argentina
Research Site
Ramos Mejia, Argentina

Research Site
Vicente Lopez, Argentina

Research Site
Rosario, Argentina

Norway
Research Site
Bergen, Norway

Research Site
Stavanger, Norway

Spain
Research Site

Lerida, Spain

Research Site
A Coruna, Spain

United States, Utah
Research Site
Salt Lake City, Utah, United States

References

Citations:

Links: URL: http://www.astrazeneca.com/node/emailtriage.aspx
Description AstraZeneca Clinical Trial Information - Outside US

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	First patient randomised 14 March 2007, last patient randomised 21 Jan 2008, data cut off data 31 March 2008

Reporting Groups

	Description
Vandetanib 100 mg Plus FOLFIRI	vandetanib 100 mg plus FOLFIRI
Vandetanib 300 mg Plus FOLFIRI	vandetanib 300 mg plus FOLFIRI
Placebo Plus FOLFIRI	placebo plus FOLFIRI

Overall Study

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
Started	35 [1]	36 [1]	35 [1]
Completed	8 [2]	7 [2]	7 [2]
Not Completed	27	29	28

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
Adverse Event	5	11	9
Condition under investigation worsened	17	13	18
Withdrawal by Subject	3	3	1
Other	2	2	0

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

Baseline Characteristics

Reporting Groups

	Description
Vandetanib 100 mg Plus FOLFIRI	vandetanib 100 mg plus FOLFIRI
Vandetanib 300 mg Plus FOLFIRI	vandetanib 300 mg plus FOLFIRI
Placebo Plus FOLFIRI	placebo plus FOLFIRI

Baseline Measures

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI	Total
Number of Participants	35	36	35	106
Age, Continuous [units: years] Mean (Full Range)	57 (39 to 80)	57 (30 to 73)	59 (37 to 73)	58 (30 to 80)
Gender, Male/Female [units: Participants]				
Female	15	13	15	43
Male	20	23	20	63

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Patients With an Objective Disease Progression Event

Measure Description	Number of patients with objective disease progression or death (by any cause in the absence of objective progression)
Time Frame	Tumour assessments carried out at screening and then as per site clinical practice until objective progression. The only additional mandatory tumour assessment visit is at the point of data cut-off (28 March 2008 +/-3 days)
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Vandetanib 100 mg Plus FOLFIRI	vandetanib 100 mg plus FOLFIRI
Vandetanib 300 mg Plus FOLFIRI	vandetanib 300 mg plus FOLFIRI
Placebo Plus FOLFIRI	placebo plus FOLFIRI

Measured Values

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
Number of Participants Analyzed	35	36	35
Number of Patients With an Objective Disease Progression Event [units: Participants]	20	24	24

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Vandetanib 100 mg Plus FOLFIRI	vandetanib 100 mg plus FOLFIRI
Vandetanib 300 mg Plus FOLFIRI	vandetanib 300 mg plus FOLFIRI
Placebo Plus FOLFIRI	placebo plus FOLFIRI

Serious Adverse Events

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	8/35 (22.86%)	13/36 (36.11%)	12/35 (34.29%)
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA [A] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)
Cardiac disorders			
ANGINA PECTORIS [A] †	1/35 (2.86%)	1/36 (2.78%)	0/35 (0%)
ATRIAL FIBRILLATION [A] †	0/35 (0%)	0/36 (0%)	2/35 (5.71%)
PERICARDIAL EFFUSION [A] †	0/35 (0%)	0/36 (0%)	1/35 (2.86%)
Gastrointestinal disorders			
DIARRHOEA [A] †	0/35 (0%)	3/36 (8.33%)	2/35 (5.71%)
GASTROINTESTINAL HAEMORRHAGE [A] †	0/35 (0%)	0/36 (0%)	2/35 (5.71%)
ILEUS [A] †	1/35 (2.86%)	0/36 (0%)	0/35 (0%)
INTESTINAL OBSTRUCTION [A] †	0/35 (0%)	0/36 (0%)	1/35 (2.86%)
PROCTITIS [A] †	1/35 (2.86%)	0/36 (0%)	0/35 (0%)
RECTAL HAEMORRHAGE [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
General disorders			
CHEST PAIN [A] †	1/35 (2.86%)	0/36 (0%)	0/35 (0%)
PYREXIA [A] †	1/35 (2.86%)	3/36 (8.33%)	3/35 (8.57%)
Infections and infestations			
BETA HAEMOLYTIC STREPTOCOCCAL INFECTION [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
CELLULITIS [A] †	1/35 (2.86%)	0/36 (0%)	0/35 (0%)
CENTRAL LINE INFECTION [A] †	1/35 (2.86%)	2/36 (5.56%)	0/35 (0%)

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
EPSTEIN-BARR VIRUS INFECTION [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
PNEUMONIA [A] †	0/35 (0%)	1/36 (2.78%)	1/35 (2.86%)
SEPSIS [A] †	0/35 (0%)	0/36 (0%)	1/35 (2.86%)
UPPER RESPIRATORY TRACT INFECTION [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
URINARY TRACT INFECTION [A] †	0/35 (0%)	0/36 (0%)	1/35 (2.86%)
VIRAL INFECTION [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
Metabolism and nutrition disorders			
HYPERGLYCAEMIA [A] †	0/35 (0%)	0/36 (0%)	1/35 (2.86%)
HYPOKALAEMIA [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
HYPONATRAEMIA [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
Renal and urinary disorders			
RENAL FAILURE [A] †	0/35 (0%)	0/36 (0%)	1/35 (2.86%)
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA [A] †	0/35 (0%)	0/36 (0%)	1/35 (2.86%)
PULMONARY EMBOLISM [A] †	0/35 (0%)	1/36 (2.78%)	0/35 (0%)
Skin and subcutaneous tissue disorders			
PHOTOSENSITIVITY REACTION [A] †	1/35 (2.86%)	0/36 (0%)	0/35 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.1

Other Adverse Events

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

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	32/35 (91.43%)	36/36 (100%)	34/35 (97.14%)
Blood and lymphatic system disorders			
ANAEMIA [A] †	1/35 (2.86%)	2/36 (5.56%)	3/35 (8.57%)
LEUKOPENIA [A] †	2/35 (5.71%)	2/36 (5.56%)	4/35 (11.43%)
NEUTROPENIA [A] †	16/35 (45.71%)	17/36 (47.22%)	19/35 (54.29%)
THROMBOCYTOPENIA [A] †	2/35 (5.71%)	6/36 (16.67%)	3/35 (8.57%)
Eye disorders			
LACRIMATION INCREASED [B] †	2/35 (5.71%)	0/36 (0%)	1/35 (2.86%)
VISION BLURRED [B] †	0/35 (0%)	1/36 (2.78%)	2/35 (5.71%)
Gastrointestinal disorders			
ABDOMINAL DISTENSION [A] †	1/35 (2.86%)	2/36 (5.56%)	1/35 (2.86%)
ABDOMINAL PAIN [A] †	6/35 (17.14%)	4/36 (11.11%)	8/35 (22.86%)
ABDOMINAL PAIN UPPER [A] †	2/35 (5.71%)	1/36 (2.78%)	3/35 (8.57%)
CONSTIPATION [A] †	7/35 (20%)	6/36 (16.67%)	7/35 (20%)
DIARRHOEA [A] †	18/35 (51.43%)	26/36 (72.22%)	17/35 (48.57%)
DRY MOUTH [A] †	0/35 (0%)	1/36 (2.78%)	2/35 (5.71%)
DYSPEPSIA [A] †	4/35 (11.43%)	6/36 (16.67%)	6/35 (17.14%)
FLATULENCE [A] †	3/35 (8.57%)	1/36 (2.78%)	0/35 (0%)
HAEMORRHOIDS [A] †	2/35 (5.71%)	0/36 (0%)	1/35 (2.86%)
NAUSEA [A] †	17/35 (48.57%)	12/36 (33.33%)	18/35 (51.43%)
ORAL PAIN [A] †	3/35 (8.57%)	1/36 (2.78%)	0/35 (0%)

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
PROCTALGIA [A] †	2/35 (5.71%)	1/36 (2.78%)	0/35 (0%)
SALIVARY HYPERSECRETION [B] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)
STOMATITIS [A] †	10/35 (28.57%)	15/36 (41.67%)	16/35 (45.71%)
TOOTHACHE [B] †	0/35 (0%)	0/36 (0%)	2/35 (5.71%)
VOMITING [A] †	9/35 (25.71%)	6/36 (16.67%)	12/35 (34.29%)
General disorders			
ASTHENIA [A] †	7/35 (20%)	6/36 (16.67%)	6/35 (17.14%)
CHILLS [A] †	1/35 (2.86%)	1/36 (2.78%)	2/35 (5.71%)
FATIGUE [A] †	10/35 (28.57%)	9/36 (25%)	9/35 (25.71%)
INJECTION SITE REACTION [A] †	2/35 (5.71%)	0/36 (0%)	1/35 (2.86%)
OEDEMA PERIPHERAL [A] †	1/35 (2.86%)	3/36 (8.33%)	3/35 (8.57%)
PYREXIA [A] †	6/35 (17.14%)	3/36 (8.33%)	3/35 (8.57%)
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA [B] †	0/35 (0%)	0/36 (0%)	2/35 (5.71%)
Infections and infestations			
CENTRAL LINE INFECTION [A] †	0/35 (0%)	4/36 (11.11%)	2/35 (5.71%)
ELECTROCARDIOGRAM QT PROLONGED [A] †	4/35 (11.43%)	8/36 (22.22%)	1/35 (2.86%)
NASOPHARYNGITIS [A] †	3/35 (8.57%)	1/36 (2.78%)	1/35 (2.86%)
SKIN INFECTION [B] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)
UPPER RESPIRATORY TRACT INFECTION [A] †	0/35 (0%)	4/36 (11.11%)	0/35 (0%)
URINARY TRACT INFECTION [A] †	1/35 (2.86%)	3/36 (8.33%)	2/35 (5.71%)

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Metabolism and nutrition disorders			
ANOREXIA [A] †	11/35 (31.43%)	10/36 (27.78%)	15/35 (42.86%)
DEHYDRATION [A] †	1/35 (2.86%)	1/36 (2.78%)	3/35 (8.57%)
HYPOKALAEMIA [A] †	1/35 (2.86%)	3/36 (8.33%)	1/35 (2.86%)
Musculoskeletal and connective tissue disorders			
ARTHRALGIA [B] †	2/35 (5.71%)	0/36 (0%)	1/35 (2.86%)
BACK PAIN [A] †	2/35 (5.71%)	4/36 (11.11%)	2/35 (5.71%)
MUSCULOSKELETAL CHEST PAIN [A] †	2/35 (5.71%)	1/36 (2.78%)	0/35 (0%)
PAIN IN JAW [B] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)
Nervous system disorders			
CHOLINERGIC SYNDROME [A] †	0/35 (0%)	2/36 (5.56%)	1/35 (2.86%)
DIZZINESS [A] †	2/35 (5.71%)	4/36 (11.11%)	4/35 (11.43%)
DYSGEUSIA [A] †	2/35 (5.71%)	2/36 (5.56%)	2/35 (5.71%)
HEADACHE [A] †	2/35 (5.71%)	3/36 (8.33%)	1/35 (2.86%)
LETHARGY [A] †	5/35 (14.29%)	2/36 (5.56%)	4/35 (11.43%)
PERIPHERAL SENSORY NEUROPATHY [A] †	2/35 (5.71%)	2/36 (5.56%)	5/35 (14.29%)
Psychiatric disorders			
ANXIETY [A] †	0/35 (0%)	3/36 (8.33%)	2/35 (5.71%)
INSOMNIA [A] †	5/35 (14.29%)	2/36 (5.56%)	0/35 (0%)
Renal and urinary disorders			
DYSURIA [A] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)
HAEMATURIA [A] †	0/35 (0%)	3/36 (8.33%)	0/35 (0%)

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Respiratory, thoracic and mediastinal disorders			
COUGH [A] †	3/35 (8.57%)	3/36 (8.33%)	3/35 (8.57%)
DYSPHONIA [A] †	1/35 (2.86%)	3/36 (8.33%)	0/35 (0%)
DYSPNOEA [A] †	1/35 (2.86%)	4/36 (11.11%)	2/35 (5.71%)
EPISTAXIS [A] †	3/35 (8.57%)	4/36 (11.11%)	2/35 (5.71%)
HAEMOTHORAX [B] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)
HICCUPS [A] †	1/35 (2.86%)	2/36 (5.56%)	2/35 (5.71%)
RHINORRHOEA [A] †	2/35 (5.71%)	1/36 (2.78%)	0/35 (0%)
Skin and subcutaneous tissue disorders			
ACNE [A] †	0/35 (0%)	2/36 (5.56%)	1/35 (2.86%)
ALOPECIA [A] †	12/35 (34.29%)	10/36 (27.78%)	15/35 (42.86%)
DERMATITIS ACNEIFORM [A] †	0/35 (0%)	2/36 (5.56%)	1/35 (2.86%)
DRY SKIN [A] †	1/35 (2.86%)	4/36 (11.11%)	2/35 (5.71%)
ERYTHEMA [A] †	2/35 (5.71%)	1/36 (2.78%)	0/35 (0%)
HYPERHIDROSIS [A] †	1/35 (2.86%)	1/36 (2.78%)	2/35 (5.71%)
NAIL DISORDER [B] †	0/35 (0%)	0/36 (0%)	2/35 (5.71%)
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME [A] †	1/35 (2.86%)	2/36 (5.56%)	2/35 (5.71%)
PHOTOSENSITIVITY REACTION [A] †	2/35 (5.71%)	0/36 (0%)	0/35 (0%)
PRURITUS [A] †	2/35 (5.71%)	5/36 (13.89%)	2/35 (5.71%)
RASH [A] †	8/35 (22.86%)	22/36 (61.11%)	6/35 (17.14%)
RASH MACULAR [B] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)

	Vandetanib 100 mg Plus FOLFIRI	Vandetanib 300 mg Plus FOLFIRI	Placebo Plus FOLFIRI
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
SKIN EXFOLIATION [A] †	0/35 (0%)	2/36 (5.56%)	0/35 (0%)
Vascular disorders			
HYPERTENSION [A] †	0/35 (0%)	4/36 (11.11%)	2/35 (5.71%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 10.1
B Term from vocabulary, MedDRA (10.1)

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.

If a study site, or an investigator, requests permission to publish data from this study, any such publication (including oral presentations) is to be agreed with AstraZeneca prior to publication

Results Point of Contact:

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