ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/30/2013

ClinicalTrials.gov ID: NCT00753714

Study Identification

Unique Protocol ID:	D4200L00012
Brief Title:	Zactima in Non Small Cell Lung Cancer (NSCLC) ELderly Patients In Combination With or Versus Gemcitabine (ZELIG)
Official Title:	Phase II, Randomised, Double-blind, Two-arm, Parallel Study of Vandetanib (ZACTIMA™ , ZD6474) Plus Gemcitabine (Gemzar®) or Gemcitabine Plus Placebo as First Line Treatment of Advanced (Stage IIIB or IV) Non Small Cell Lung Cancer (NSCLC) Elderly Patients.
Secondary IDs:	EUDRACT n° 2007-004521-22

Study Status

Record Verification:	January 2013
Overall Status:	Completed
Study Start:	October 2008
Primary Completion:	April 2011 [Actual]
Study Completion:	December 2011 [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: Prot. uscita n° 0016394 Board Name: Comitato Etico dell'Azienda Ospedaliera S. Giuseppe Moscati di Avellino Board Affiliation: Azienda Ospedaliera S. Giuseppe Moscati di Avellino Phone: +39 0825203013 Email: comitatoeticoav@gmail.com
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Italy: Ethics Committee

Study Description

Brief Summary:	The primary objective of this study is to demonstrate an improvement in Progression-Free Survival (PFS) for the combination of vandetanib plus gemcitabine compared with gemcitabine plus placebo in chemonaïve (not including an adjuvant regimen) patients aged ≥ 70 years with advanced NSCLC.
Detailed Description:	

Conditions

Conditions:	Non Small Cell Lung Cancer
Keywords:	ZD6474 VANDETANIB ZACTIMA ADVANCED NSCLC LUNG CANCER ELDERLY PATIENTS GEMCITABINE PHASE II RANDOMIZED DOUBLE-BLIND histologically or cytologically-confirmed advanced (stage IIIB with supraclavicular lymph node metastases or pleural effusion or stage IV) NSCLC

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Efficacy Study
Enrollment:	124 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: A Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1.Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.	Drug: ZD6474, Vandetanib 100 mg as a once daily oral dose, from Day 1 until disease progression or unacceptable toxicity or consent withdrawal whichever occurs first Other Names: • Zactima Drug: Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle UP to 6 cycles or UNTIL disease progression or unacceptable toxicity or consent withdrawal whichever occurs first Other Names: • Gemzar
Placebo Comparator: B Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1.Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.	Drug: Placebo to Match ZD6474, Vandetanib 100 mg as a once daily oral dose, from Day 1 UNTIL disease progression or unacceptable toxicity or consent withdrawal whichever occurs first Other Names: • Zactima Drug: Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle UP to 6 cycles or UNTIL disease progression or unacceptable toxicity or consent withdrawal whichever occurs first Other Names:

Arms	Assigned Interventions
	• Gemzar

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 70 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Histologic or cytologic confirmation of advanced NSCLC (stage IIIB with supraclavicular lymph node metastases or pleural effusion or stage IV) on entry into study
- One or more measurable lesions at least 10 mm in the longest diameter (LD) by spiral CT scan or 20 mm with conventional techniques according to RECIST criteria
- Chemotherapy-naïve (prior chemotherapy in the adjuvant setting completed more than 3 months before the trial entry is accepted).
- Female or male aged 70 years or above

Exclusion Criteria:

- Patients must not have received prior anti-cancer therapy except in the adjuvant setting
- Inadequate end-organ function or Evidence of severe or uncontrolled systemic disease or any concurrent condition which in the Investigator’s opinion makes it undesirable for the patient to participate in the trial
- Significant cardiovascular event (e.g. myocardial infarction, superior vena cava [SVC] syndrome, New York Heart Association [NYHA] classification of heart disease ³2) within 3 months before entry, or presence of cardiac disease that in the opinion of
- History of arrhythmia or QTc with Bazett’s correction unmeasurable or ≥ 480 msec on screening ECG

Contacts/Locations

Study Officials: Cesare Gridelli, MD
Study Chair
A.O. S.Giuseppe Moscati di Avellino - AVELLINO ITALY

Fortunato Ciardiello, MD
Study Principal Investigator

Seconda Università di Napoli - NAPOLI ITALY

Peter Langmuir, MD
Study Director
AstraZeneca

Locations: Italy

Research Site
Avellino, AV, Italy

Research Site
Bari, BA, Italy

Research Site
Bologna, BO, Italy

Research Site
Genova, GE, Italy

Research Site
Meldola, (fc), Italy

Research Site
Milano, MI, Italy

Research Site
Orbassano, TO, Italy

Research Site
Padova, Italy

Research Site
Perugia, PG, Italy

Research Site
Ravenna, RA, Italy

Research Site
Roma, Roma, Italy

Research Site
Taormina, ME, Italy

Research Site
Trento, TN, Italy

Research Site
Treviglio, BG, Italy

Research Site
Udine, UD, Italy

References

Citations: Gridelli C. Treatment of advanced non small-cell lung cancer in the elderly: from best supportive care to the combination of platin-based chemotherapy and targeted therapies. J Clin Oncol. 2008 Jan 1;26(1):13-5. doi: 10.1200/JCO.2007.14.1820. PubMed 18165633

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	A total of 124 patients have been enrolled in a period of 19 months in 17 actively recruiting Oncologic Medical Department in Italy.

Reporting Groups

	Description
ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1. Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.
Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1. Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued

Overall Study

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine
Started	61	63
Completed	1	1
Not Completed	60	62
Lack of Efficacy	21	34
Adverse Event	26	18
Protocol Violation	1	0
Lost to Follow-up	0	1
Withdrawal by Subject	2	1
Death	3	3
not specified	7	5

Baseline Characteristics

Reporting Groups

	Description
ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.
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Baseline Measures

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Total
Number of Participants	61	63	124

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Total
Age, Continuous [units: years] Mean (Standard Deviation)	75.03 (3.34)	75.48 (3.49)	75.25 (3.41)
Gender, Male/Female [units: Participants]			
Female	16	18	34
Male	45	45	90

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Progression Free Survival
Measure Description	
Time Frame	Oct 2008- dec 2011
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1.Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.
Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued

Measured Values

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine
Number of Participants Analyzed	61	63
Progression Free Survival [units: days] Median (95% Confidence Interval)	183 (116 to 214)	169 (95 to 194)

2. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	
Time Frame	Oct 2008- dec 2011
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued
Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued

Measured Values

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine
Number of Participants Analyzed	61	63
Overall Survival [units: days]	262 (170 to 356)	305 (214 to 355)

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine
Median (95% Confidence Interval)		

3. Secondary Outcome Measure:

Measure Title	Overall Objective Response
Measure Description	
Time Frame	Oct 2008- dec 2011
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
ZD6474 ((Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.
Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.

Measured Values

	ZD6474 ((Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine
Number of Participants Analyzed	61	63
Overall Objective Response [units: Participants]	9	8

4. Secondary Outcome Measure:

Measure Title	Duration of Response
Measure Description	
Time Frame	Oct 2008- dec 2011
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued
Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued

Measured Values

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine
Number of Participants Analyzed	61	63
Duration of Response [units: days] Median (95% Confidence Interval)	225 (175 to NA) [1]	214 (124 to 232)

[1] Too few participants experienced event to compute upper limit of CI, i.e.sample analyzed is to small compared with the initial statistical plan or when less than 50% of the subjects are available for analysis

5. Secondary Outcome Measure:

Measure Title	The Safety and Tolerability Profile of ZD6474 (Vandetanib) in Combination With Gemcitabine

Measure Description	The Safety and Tolerability Profile of ZD6474 (Vandetanib) in Combination With Gemcitabine is defined as the number of Adverse Events which includes any symptoms and/or Clinically Significant Laboratory or Vital Signs Abnormalities, and/or ECGs Changes
Time Frame	Oct 2008- Dec 2011
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued
Placebo to Match ZD6474 (Vandetanib),Gemcitabine	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.

Measured Values

	ZD6474 (Vandetanib),Gemcitabine	Placebo to Match ZD6474 (Vandetanib),Gemcitabine
Number of Participants Analyzed	61	63
The Safety and Tolerability Profile of ZD6474 (Vandetanib) in Combination With Gemcitabine [units: Adverse Events]	378	381

Reported Adverse Events

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

Reporting Groups

	Description
ZD6474 (Gemcitabine), Vandetanib	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with vandetanib alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued.
Placebo to Match ZD6474 (Gemcitabine), Vandetanib	Gemcitabine administered intravenously at 1200 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1. . Patients will receive gemcitabine for up to a maximum of 6 cycles, after which period patients should continue on daily oral dosing with placebo alone until progression. Once a patient has met the study criteria for disease progression on vandetanib/gemcitabine or placebo/gemcitabine, randomised treatment must be permanently discontinued

Serious Adverse Events

	ZD6474 (Gemcitabine), Vandetanib	Placebo to Match ZD6474 (Gemcitabine), Vandetanib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	26/61 (42.62%)	25/63 (39.68%)
Blood and lymphatic system disorders		
Pancytopenia [A] †	1/61 (1.64%)	0/63 (0%)
Cardiac disorders		
Cardiac Failure Acute [A] *	1/61 (1.64%)	0/63 (0%)
Myocardial infarction [B] †	1/61 (1.64%)	0/63 (0%)
Pleuropericarditis [A] *	1/61 (1.64%)	0/63 (0%)
tachycardia [B] †	0/61 (0%)	1/63 (1.59%)
Eye disorders		
Eye Disorder [A] *	1/61 (1.64%)	0/63 (0%)
Gastrointestinal disorders		
Ascites [A] *	0/61 (0%)	1/63 (1.59%)
Dysphagia [A] *	0/61 (0%)	1/63 (1.59%)
Pancreatitis [A] *	1/61 (1.64%)	0/63 (0%)

	ZD6474 (Gemcitabine), Vandetanib	Placebo to Match ZD6474 (Gemcitabine), Vandetanib
	Affected/At Risk (%)	Affected/At Risk (%)
Vomiting [A] *	1/61 (1.64%)	0/63 (0%)
General disorders		
Chest Pain [A] *	0/61 (0%)	1/63 (1.59%)
Pyrexia [A] *	0/61 (0%)	3/63 (4.76%)
Hepatobiliary disorders		
Hepatic Cirrhosis [A] *	0/61 (0%)	1/63 (1.59%)
Infections and infestations		
Pneumonia [A] *	2/61 (3.28%)	1/63 (1.59%)
Urinary Tract Infection [A] *	1/61 (1.64%)	0/63 (0%)
Injury, poisoning and procedural complications		
Femur Fracture [A] *	1/61 (1.64%)	0/63 (0%)
Investigations		
Weight Decrease [A] *	1/61 (1.64%)	0/63 (0%)
Musculoskeletal and connective tissue disorders		
Muscoloskeletal Pain [A] *	1/61 (1.64%)	0/63 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Ear Neoplasm [A] *	1/61 (1.64%)	0/63 (0%)
Malignant Melanoma [A] *	0/61 (0%)	1/63 (1.59%)
Oesophageal Adenocarcinoma [A] *	0/61 (0%)	1/63 (1.59%)
Nervous system disorders		
Cerebral Infarction [A] *	1/61 (1.64%)	0/63 (0%)
Cerebral Ischemia [A] *	0/61 (0%)	2/63 (3.17%)
Depressed Level Of Consciuosness [A] †	1/61 (1.64%)	0/63 (0%)

	ZD6474 (Gemcitabine), Vandetanib	Placebo to Match ZD6474 (Gemcitabine), Vandetanib
	Affected/At Risk (%)	Affected/At Risk (%)
Presyncope [A] *	0/61 (0%)	1/63 (1.59%)
Psychiatric disorders		
Confusional State [A] †	1/61 (1.64%)	1/63 (1.59%)
Renal and urinary disorders		
Renal Failure [A] †	2/61 (3.28%)	0/63 (0%)
Uraniry Retention [A] *	0/61 (0%)	1/63 (1.59%)
Respiratory, thoracic and mediastinal disorders		
Acute Respiratory Failure [A] *	0/61 (0%)	1/63 (1.59%)
Cough [A] *	1/61 (1.64%)	0/63 (0%)
Dyspnoea [A] *	3/61 (4.92%)	9/63 (14.29%)
Pleural Effusion [A] *	1/61 (1.64%)	0/63 (0%)
Pleurisy [A] *	1/61 (1.64%)	1/63 (1.59%)
Pneumonitis [A] †	2/61 (3.28%)	0/63 (0%)
Pneumothorax [A] *	1/61 (1.64%)	0/63 (0%)
Pulmunary Oedema [A] *	2/61 (3.28%)	0/63 (0%)
Pulmunary embolism [A] *	3/61 (4.92%)	3/63 (4.76%)
Respiratory Distress [A] *	1/61 (1.64%)	0/63 (0%)
acute pulmunary oedema [A] *	1/61 (1.64%)	0/63 (0%)
chronic obstructive pulmunary disease [A] *	1/61 (1.64%)	0/63 (0%)
respiratory failure [A] *	2/61 (3.28%)	1/63 (1.59%)
Skin and subcutaneous tissue disorders		
Skin Toxicity [A] †	1/61 (1.64%)	0/63 (0%)

	ZD6474 (Gemcitabine), Vandetanib	Placebo to Match ZD6474 (Gemcitabine), Vandetanib
	Affected/At Risk (%)	Affected/At Risk (%)
rash [A] †	1/61 (1.64%)	0/63 (0%)
Vascular disorders		
Infarction [A] *	0/61 (0%)	1/63 (1.59%)
Peripheral Ischaemia [A] *	0/61 (0%)	1/63 (1.59%)
Vena Cava Thrombosis [A] *	0/61 (0%)	1/63 (1.59%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 12.0
B Term from vocabulary, MedDRA 10.0

Other Adverse Events

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

	ZD6474 (Gemcitabine), Vandetanib	Placebo to Match ZD6474 (Gemcitabine), Vandetanib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	59/61 (96.72%)	62/63 (98.41%)
Blood and lymphatic system disorders		
Alanine Aminotransferase Increased [A] †	5/61 (8.2%)	1/63 (1.59%)
Anaemia [A] †	8/61 (13.11%)	14/63 (22.22%)
Aspartate Aminotransferase Inctìreased [A] †	4/61 (6.56%)	1/63 (1.59%)
Neutropenia [A] †	12/61 (19.67%)	12/63 (19.05%)
Neutrphil Count Decreased [B] †	5/61 (8.2%)	2/63 (3.17%)
PLT count decrease [A] †	7/61 (11.48%)	9/63 (14.29%)
Thrombocytopenia [A] †	7/61 (11.48%)	4/63 (6.35%)
Gastrointestinal disorders		
Constipation [A] *	2/61 (3.28%)	4/63 (6.35%)

	ZD6474 (Gemcitabine), Vandetanib	Placebo to Match ZD6474 (Gemcitabine), Vandetanib
	Affected/At Risk (%)	Affected/At Risk (%)
Diarrhoea [A] *	9/61 (14.75%)	9/63 (14.29%)
Nausea [A] *	7/61 (11.48%)	8/63 (12.7%)
Vomiting [A] *	4/61 (6.56%)	7/63 (11.11%)
General disorders		
Asthenia [A] *	9/61 (14.75%)	13/63 (20.63%)
Chest Pain [B] *	2/61 (3.28%)	15/63 (23.81%)
Fatigue [A] *	14/61 (22.95%)	15/63 (23.81%)
Mucosal Inflammation [A] *	4/61 (6.56%)	4/63 (6.35%)
Oedema Peripheral [A] *	4/61 (6.56%)	12/63 (19.05%)
pyrexia [A] *	17/61 (27.87%)	17/63 (26.98%)
Metabolism and nutrition disorders		
Anorexia [A] *	8/61 (13.11%)	17/63 (26.98%)
Hypokaliemia [A] †	2/61 (3.28%)	7/63 (11.11%)
Psychiatric disorders		
Depression [A] *	3/61 (4.92%)	4/63 (6.35%)
Insomnia [A] *	1/61 (1.64%)	4/63 (6.35%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	9/61 (14.75%)	10/63 (15.87%)
Dispnoea [A] *	13/61 (21.31%)	19/63 (30.16%)
Pulmunary Embolism [A] *	4/61 (6.56%)	3/63 (4.76%)
Respiratory Failure [A] *	4/61 (6.56%)	1/63 (1.59%)
Skin and subcutaneous tissue disorders		

	ZD6474 (Gemcitabine), Vandetanib	Placebo to Match ZD6474 (Gemcitabine), Vandetanib
	Affected/At Risk (%)	Affected/At Risk (%)
Pruritus [A] *	4/61 (6.56%)	2/63 (3.17%)
Rash [A] *	15/61 (24.59%)	5/63 (7.94%)
Vascular disorders		
Phlebitis [A] *	5/61 (8.2%)	3/63 (4.76%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 12.0
B Term from vocabulary, MedDRA 10.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

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