ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 12/19/2013

ClinicalTrials.gov ID: NCT00753675

Study Identification

Unique Protocol ID:	D4200L00007
Brief Title:	Vandetanib Gemcitabine Or Placebo Plus Gemcitabine Or Vandetanib Monotherapy In Advanced Biliary Tract Cancer (VANGOGH)
Official Title:	A Randomized, Multicentre, Phase II, Parallel-Group Trial of Vandetanib Monotherapy or Vandetanib in Combination With Gemcitabine Versus Gemcitabine Plus Vandetanib Matching Placebo in Subjects With Advanced Biliary Tract Cancer (Gallbladder Cancer, Cancer of the Extrahepatic Bile Duct, Intrahepatic Cholangiocarcinoma and Ampullary Carcinoma)
Secondary IDs:	EUDRACT n° 2007-003056-12

Study Status

Record Verification:	December 2013
Overall Status:	Completed
Study Start:	October 2008
Primary Completion:	September 2012 [Actual]
Study Completion:	September 2012 [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: CE ICH - P.U. -01/08 Board Name: COMITATO ETICO DELL'IRCCS ISTITUTO CLINICO HUMANITAS DI ROZZANO (MI) Board Affiliation: IRCCS ISTITUTO CLINICO HUMANITAS DI ROZZANO (MI) Phone: +39 0282247216 Email: comitato.etico@humanitas.it
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Italy: Ethics Committee

Study Description

Brief Summary:	The primary objective of the trial is to determine the efficacy of VANDETANIB monotherapy or VANDETANIB plus GEMCITABINE or PLACEBO plus GEMCITABINE in prolonging the progression-free survival (PFS) at the trial closure in patients with advanced (unresectable or metastatic) biliary tract cancer.
Detailed Description:	

Conditions

Conditions:	Biliary Tract Cancer Gallbladder Cancer Cancer Of The Extrahepatic Bile Duct Ampullary Carcinoma
Keywords:	Intrahepatic Cholangiocarcinoma Vandetanib Zactima Advanced Biliary Tract Gallbladder Extrahepatic Bile Duct

Intrahepatic Cholangiocarcinoma
Ampullary Carcinoma

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	3
Masking:	Double Blind (Subject, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Efficacy Study
Enrollment:	174 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: A Vandetanib 300 mg as a once daily oral dose, from Day 1	Drug: ZD6474, Vandetanib 300 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
Experimental: B Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)	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 1000 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: C	Drug: Gemcitabine

Arms	Assigned Interventions
Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).	administered intravenously at 1000 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 Drug: Placebo matching ZD6474 Placebo to match ZD6474 100 mg as a once daily oral dose, from Day 1 until disease progression or unacceptable toxicity or consent withdrawal whichever occurs first

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Histologically or cytologically-confirmed advanced (unresectable or metastatic) biliary tract cancer (gallbladder cancer, cancer of the extrahepatic bile duct, intrahepatic cholangiocarcinoma and ampullary carcinoma)
- Patients must have measurable or evaluable but non-measurable disease
- Chemotherapy-naïve (prior chemotherapy in the adjuvant setting completed more than 3 months before the trial entry is accepted).
- WHO performance status 0 to 2: patients must have a WHO PS ≤ 2

Exclusion Criteria:

- Patients must not have received prior systemic therapy for advanced (unresectable or metastatic) disease; prior chemotherapy in the adjuvant setting within 3 months before the trial entry is accepted
- 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 or which would jeopardize compliance wit
- 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: Armando Santoro, MD
Study Chair
Istituto Clinico Humanitas - ROZZANO (MI) ITALY

Lorenza Rimassa, MD
Study Principal Investigator
Istituto Clinico Humanitas - ROZZANO (MI) ITALY

Peter Langmuir, MD
Study Director
AstraZeneca

Locations: Italy
Research Site
Ancona, Italy

Research Site
Aviano, PN, Italy

Research Site
Brescia, BS, Italy

Research Site
Firenze, FI, Italy

Research Site
Genova, GE, Italy

Research Site
Livorno, Italy

Research Site
Milano, Mi, Italy

Research Site
Palermo, PA, Italy

Research Site
Parma, PR, Italy

Research Site
Pisa, Italy

Research Site
Reggio Emilia, RE, Italy

Research Site
Torino, Italy

Research Site
Napoli, Italy

Research Site
Ravenna, Italy

Research Site
Rho, Italy

References

Citations: Wedge SR et al 2002Wedge SR, Ogilvie DJ, Dukes M, Kendrew J, Chester R, Jackson JA, et al. ZD6474 inhibits vascular endothelial growth factor signaling, angiogenesis, and tumour growth following oral administration. Cancer Res 2002; 62(16):4645-55.

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	180 subjects were screened at 19 sites and 174 were randomized

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)

	Description
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Overall Study

	Arm A Vandetanib 300 mg	Arm B Vandetanib 100mg + Gemcitab	ARM C Placebo + Gemcitabine
Started	59	59	56
Completed	0	0	0
Not Completed	59	59	56
other reason	11	12	13
Death	1	2	4
Adverse Event	11	9	4
Objective progression of disease	35	35	35
Withdrawal by Subject	0	1	0
Lost to Follow-up	1	0	0

Baseline Characteristics

Analysis Population Description

Patient screened 180 Patient Randomized 174 (1 never treated) Sceening failures 6 Patient Treated 173 (ITT=165 ; 8 excluded from ITT due to missing postbaseline assesment)

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)

	Description
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Baseline Measures

	Arm A Vandetanib 300 mg	Arm B Vandetanib 100mg + Gemcitab	ARM C Placebo+ Gemcitabine	Total
Number of Participants	59	58	56	173
Age, Continuous [1] [units: years] Mean (Standard Deviation)	62.39 (10.108)	64.41 (9.455)	63.95 (8.764)	63.57 (9.456)
Gender, Male/Female [1] [units: participants]				
Female	34	27	31	92
Male	25	31	25	81

[1] Safety Population

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Progression Free Survival
Measure Description	Progression was defined as Time from the date of first dose of study medication to progression of disease, or death (it also includes patients who are lost to follow-up or have withdrawn consent) and evaluated with RECIST criteria as an increase of at least 20% in the sum of longest diameter (LD) of target lesion(s) taking as reference the smallest sum of LD since the treatment started or any new lesion(s).
Time Frame	up to 1032 days
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Measured Values

	Arm A Vandetanib 300 mg	Arm B Vandetanib 100mg + Gemcitab	ARM C Placebo + Gemcitabine
Number of Participants Analyzed	56	57	52
Progression Free Survival [units: days] Median (95% Confidence Interval)	105 (72 to 155)	114 (91 to 193)	148 (72 to 225)

2. Secondary Outcome Measure:

Measure Title	Objective Tumor Response Rate (CR+PR),
Measure Description	Objective Tumor Response Rate was defined as complete response (CR) + partial response (PR) evaluated by RECIST. CR was defined as disappearance of all target lesions. PR was defined as at least 30% decrease in the sum of longest diameters (LD) of target lesion(s) taking as reference the baseline sum of LD
Time Frame	up to 1032 days
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1

	Description
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Measured Values

	Arm A Vandetanib 300 mg	Arm B Vandetanib 100mg + Gemcitab	ARM C Placebo + Gemcitabine
Number of Participants Analyzed	56	57	52
Objective Tumor Response Rate (CR+PR), [units: Participants]			
Objective Response = NO	54	46	45
Objective Response = YES	2	11	7

3. Secondary Outcome Measure:

Measure Title	Disease Control Rate (CR+PR+SD)
Measure Description	DCR is the sum of patients with a best overall CR, PR or SD (>=8 weeks) by the patient in the analysis
Time Frame	up to 1032 days
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1

	Description
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Measured Values

	Arm A Vandetanib 300 mg	Arm B Vandetanib 100mg + Gemcitab	ARM C Placebo + Gemcitabine
Number of Participants Analyzed	56	57	52
Disease Control Rate (CR+PR+SD) [units: Partecipants]			
Disease control rate = NO	42	40	32
Disease control rate = YES	14	17	20

4. Secondary Outcome Measure:

Measure Title	Duration of Response (DOR)
Measure Description	DOR is defined from the date of first documentation of response until date of PD or death
Time Frame	up to 1032 days
Safety Issue?	No

Analysis Population Description

ITT (best response of CR or PR only)

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1

	Description
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Measured Values

	Arm A Vandetanib 300 mg	Arm B Vandetanib 100mg + Gemcitab	ARM C Placebo + Gemcitabine
Number of Participants Analyzed	2	11	7
Duration of Response (DOR) [units: Days] Median (95% Confidence Interval)	277 (267 to 286)	179 (85 to 369)	127 (85 to 152)

5. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	OS is defined from the date of randomization to death
Time Frame	up to 1032 days
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)

	Description
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Measured Values

	Arm A Vandetanib 300 mg	Arm B Vandetanib 100mg + Gemcitab	ARM C Placebo + Gemcitabine
Number of Participants Analyzed	56	57	52
Overall Survival [units: Days] Median (95% Confidence Interval)	228 (190 to 364)	284 (213 to 359)	307 (254 to 523)

Reported Adverse Events

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

Reporting Groups

	Description
Arm A Vandetanib 300 mg	Vandetanib 300 mg as a once daily oral dose, from Day 1
Arm B Vandetanib 100mg + Gemcitab	Gemcitabine administered intravenously at 1000 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 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy)
ARM C Placebo+ Gemcitabine	Gemcitabine administered intravenously at 1000 mg/m2 over 30 minutes on Days 1 and 8 of each 21-day cycle up to 6 cycles plus Vandetanib 100 mg Matching Placebo orally once-daily, from Day 1 (after 6 cycles, in the absence of disease progression or unacceptable toxicity, Investigators remain at liberty to continue Gemcitabine plus Vandetanib / Placebo or to continue Vandetanib / Placebo monotherapy).

Serious Adverse Events

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	16/59 (27.12%)		15/58 (25.86%)		12/56 (21.43%)	
Blood and lymphatic system disorders						
Disseminated Intravascular [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Pancytopenia [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Thrombocytopenia [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Cardiac disorders						
Acute Myocardial Infarction [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Cardiac Failure Acute [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Torsade de Pointes [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Gastrointestinal disorders						
Abdominal Pain †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Ascites [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0
Duodenal Obstruction [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Intestinal Obstruction [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Nausea [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Vomiting [A] †	3/59 (5.08%)	3	0/58 (0%)	0	2/56 (3.57%)	2
General disorders						
Asthenia [C] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Condition Aggravated [C] †	0/59 (0%)	0	1/58 (1.72%)	1	1/56 (1.79%)	1
Fatigue [C] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
General Physical Health Deterioration [C] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Pyrexia [C] †	3/59 (5.08%)	3	0/58 (0%)	0	2/56 (3.57%)	2
Hepatobiliary disorders						
Acute Hepatic Failure [C] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Cholangites [C] †	1/59 (1.69%)	1	1/58 (1.72%)	1	1/56 (1.79%)	1
Hepatic Failure [C] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Hyperbilirubineamia [C] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Jaundice [C] †	0/59 (0%)	0	2/58 (3.45%)	2	2/56 (3.57%)	2
Infections and infestations						
Pneumonia [C] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Investigations						
Blood Bilirubin [C] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Blood Bilirubin increased [C] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Electrocardiogram Repolarisation Abnormaly [C] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Metabolism and nutrition disorders						
Cachexia [C] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Dehydration [C] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Metabolic Acidosis [C] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Musculoskeletal and connective tissue disorders						
Back Pain [C] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Nervous system disorders						
Epilepsy [C] †	2/59 (3.39%)	2	0/0	0	0/0	0
Renal and urinary disorders						

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Oliguria [C] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Renal Failure [C] †	0/59 (0%)	0	2/58 (3.45%)	2	1/56 (1.79%)	1
Renal Failure Acute [C] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Respiratory, thoracic and mediastinal disorders						
Dyspnoea [C] †	1/59 (1.69%)	1	2/58 (3.45%)	2	0/56 (0%)	0
Pleural Effusion [C] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Pulmonary Hypertension [C] †	0/59 (0%)	0	2/58 (3.45%)	2	0/56 (0%)	0
Pulmonary embolism [C] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Vascular disorders						
Hypertension [C] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Hypotension [C] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.0
B Term from vocabulary, MeDra
C Term from vocabulary, MeDRA 15.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 1%

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	57/59 (96.61%)		53/58 (91.38%)		50/56 (89.29%)	
Blood and lymphatic system disorders						
Anemia [A] †	1/59 (1.69%)	4	10/58 (17.24%)	20	7/56 (12.5%)	18

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Anemia macrocytic [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Autoimmune thrombocytopenia [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Dessemintaed Intracascula Coagulation [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Hyperbilirubineamia [B] †	0/59 (0%)	0	1/58 (1.72%)	2	0/56 (0%)	0
Iron deficency anemia [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Leukcytosis [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Leukopenia [B] †	0/59 (0%)	0	3/58 (5.17%)	6	6/56 (10.71%)	17
Neutropenia [B] †	0/59 (0%)	0	7/58 (12.07%)	15	10/56 (17.86%)	28
Pancytopenia [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Platelet production decreased [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Thrombocytopenia [B] †	2/59 (3.39%)	2	5/58 (8.62%)	7	2/56 (3.57%)	2
Thrombocytosis [A] †	0/59 (0%)	0	1/58 (1.72%)	1	1/56 (1.79%)	1
White blood cell disorder [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Cardiac disorders						
Acute Myocardial Infarction [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Arrhytmia [B] †	1/59 (1.69%)	2	0/58 (0%)	0	0/56 (0%)	0
Atrial Fibrillation [B] †	1/59 (1.69%)	1	1/58 (1.72%)	2	1/56 (1.79%)	1
Bundle Branch block right [B] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0
Bundle branch block [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Cardiac Failure [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Cardiac Failure Acute [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Extrasystoles [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Oedema peripheral [B] †	0/59 (0%)	0	2/58 (3.45%)	2	0/56 (0%)	0
Sinus tachycardia [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Tachycardia [B] †	2/59 (3.39%)	2	1/58 (1.72%)	1	0/56 (0%)	0
Torsade de pointes [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Ear and labyrinth disorders						
Vertigo [B] †	2/59 (3.39%)	2	0/58 (0%)	0	0/56 (0%)	0
Endocrine disorders						
Diabete Mellitus [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Hyperglycamia [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Eye disorders						
Conjunctival hemorrhage [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Eye pruritus [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Ocular icterus [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Periorbital Oedema [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Gastrointestinal disorders						
Abdominal Distension [A] †	1/59 (1.69%)	1	0/58 (0%)	0	2/56 (3.57%)	3
Abdominal Pain upper [B] †	3/59 (5.08%)	3	6/58 (10.34%)	6	6/56 (10.71%)	6
Abdominal mass [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Abdominal pain [B] †	15/59 (25.42%)	16	8/58 (13.79%)	9	14/56 (25%)	17
Aborectal discomfort [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Ascites [B] †	4/59 (6.78%)	4	2/58 (3.45%)	2	2/56 (3.57%)	3
Constipation [B] †	2/59 (3.39%)	2	3/58 (5.17%)	3	9/56 (16.07%)	9
Diarrhoea [B] †	15/59 (25.42%)	32	6/58 (10.34%)	13	8/56 (14.29%)	10
Dry mouth [B] †	2/59 (3.39%)	2	0/58 (0%)	0	0/56 (0%)	0
Duodenal obstruction [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Dysgeusia [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Dyshagia [B] †	1/59 (1.69%)	2	0/58 (0%)	0	0/56 (0%)	0
Dyspepsia [B] †	1/59 (1.69%)	1	1/58 (1.72%)	1	2/56 (3.57%)	4
Gastroesophageal reflux disease [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Gastrointestinal toxicity [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Gingivitis [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Haemorrhoids [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Hiccups [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Intestinal Obstruction [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Nausea [B] †	5/59 (8.47%)	6	6/58 (10.34%)	7	17/56 (30.36%)	29
Oral Mucosal erythema [B] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Pelvic Pain [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Proctitis [B] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Stomatitis [B] †	1/59 (1.69%)	1	1/58 (1.72%)	1	3/56 (5.36%)	3
Vomiting [B] †	8/59 (13.56%)	11	5/58 (8.62%)	7	9/56 (16.07%)	21

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
proctalgia [B] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
General disorders						
Asthenia [A] [1] †	7/59 (11.86%)	7	14/58 (24.14%)	17	15/56 (26.79%)	20
Chest Pain [B] †	3/59 (5.08%)	3	2/58 (3.45%)	2	1/56 (1.79%)	2
Chills [A] †	1/59 (1.69%)	1	1/58 (1.72%)	2	0/56 (0%)	0
Condition aggravated [B] †	0/59 (0%)	0	2/58 (3.45%)	2	2/56 (3.57%)	2
Fatigue [B] †	8/59 (13.56%)	9	7/58 (12.07%)	9	8/56 (14.29%)	11
General physical health deterioration [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Gravitational oedema [B] †	2/59 (3.39%)	2	1/58 (1.72%)	1	1/56 (1.79%)	1
Hyperhidrosis [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Hyperpyrexia [B] †	2/59 (3.39%)	2	0/58 (0%)	0	2/56 (3.57%)	2
Malaise [C] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Mucosal Inflammation [C] †	4/59 (6.78%)	4	4/58 (6.9%)	6	0/56 (0%)	0
Multi organ failure [C] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Oedema [C] †	0/59 (0%)	0	0/58 (0%)	0	3/56 (5.36%)	3
Oedema Peripheral [C] †	2/59 (3.39%)	2	3/58 (5.17%)	9	1/56 (1.79%)	3
Pain [D] †	2/59 (3.39%)	2	3/58 (5.17%)	4	1/56 (1.79%)	2
Pyrexia [D] †	8/59 (13.56%)	10	14/58 (24.14%)	22	14/56 (25%)	22
Hepatobiliary disorders						
Acute Hepatic Failure [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Ascites [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Bile Duct Obstruction [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Cholangites [A] †	3/59 (5.08%)	3	2/58 (3.45%)	3	3/56 (5.36%)	3
Hepatic Failure [A] †	0/59 (0%)	0	1/58 (1.72%)	1	1/56 (1.79%)	1
Hepatic pain [B] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Hyperbilirubinaemia [A] †	4/59 (6.78%)	10	5/58 (8.62%)	10	3/56 (5.36%)	3
Hypertrasaminasaemia [A] †	2/59 (3.39%)	3	2/58 (3.45%)	2	2/56 (3.57%)	2
Hypoalbuminaemia [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Jaundice [A] †	2/59 (3.39%)	3	3/58 (5.17%)	3	3/56 (5.36%)	3
Liver injury [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Immune system disorders						
Contrast media allergy [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Dermatitis allergic [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Seasonal allergy [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Infections and infestations						
Bacterial Rhinitis [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Cystis escherichia [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Folliculitis [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Hepatobiliary infection [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Influenza [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Nasopharyngitis [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Oral Herpes [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Pneumonia [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Skin Infection [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Tooth abcess [A] †	0/59 (0%)	0	0/58 (0%)	0	2/56 (3.57%)	3
Urinary tract infection [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0
Viral infection [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Injury, poisoning and procedural complications						
Spinal Fracture [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Investigations						
Alanine aminotransferase [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Alanine aminotransferase increased [A] †	1/59 (1.69%)	1	2/58 (3.45%)	2	1/56 (1.79%)	1
Aspartate aminotranferase [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Asparteate amonotranferase increased [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Blood Bilirubin [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Blood Bilirubin increased [A] †	3/59 (5.08%)	5	1/58 (1.72%)	1	0/56 (0%)	0
Blood alkaline phosphatase [A] †	2/59 (3.39%)	2	0/58 (0%)	0	0/56 (0%)	0
Blood creatine [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Blood creatinine increased [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Blood glucose decreased [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Blood lactate dehdrogenase increased [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Blood potassium increased [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Blood urea increased [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Electrocardiogram QT prolonged [A] †	2/59 (3.39%)	2	2/58 (3.45%)	2	1/56 (1.79%)	1
Electrocardiogram T wave inversion [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Electrocardiogram abnormal [A] †	2/59 (3.39%)	3	0/58 (0%)	0	0/56 (0%)	0
Electrocardiogram repolarisation abnormaly [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0
Gamma -glumayltransferase [A] †	2/59 (3.39%)	2	0/58 (0%)	0	0/56 (0%)	0
Gamma-glutamyltransferase increased [A] †	0/59 (0%)	0	1/58 (1.72%)	2	3/56 (5.36%)	5
International normalised ratio increased [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Platelet count decreased [A] †	0/59 (0%)	0	3/58 (5.17%)	3	0/56 (0%)	0
Platelet count increased [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Transaminase increased [A] †	1/59 (1.69%)	2	1/58 (1.72%)	2	0/56 (0%)	0
Urine colour abnormal [B] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Weight decreased [A] †	2/59 (3.39%)	2	1/58 (1.72%)	1	0/56 (0%)	0
Metabolism and nutrition disorders						
Cachexia [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Decreased appetite [A] †	5/59 (8.47%)	5	8/58 (13.79%)	10	4/56 (7.14%)	4
Deydratation [A] †	2/59 (3.39%)	2	1/58 (1.72%)	1	0/56 (0%)	0
Hyperbilirubinaemia [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Hypercalcemia [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Hypercreatininaemia [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Hyperglycaemia [A] †	0/59 (0%)	0	2/58 (3.45%)	2	1/56 (1.79%)	1
Hypoalbuminaemia [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Hypocalcaemia [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Hypoglycaemia [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Hypokalaemia [A] †	0/59 (0%)	0	2/58 (3.45%)	2	0/56 (0%)	0
Metabolic Acidosis [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Musculoskeletal and connective tissue disorders						
Arthralgia [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	5/56 (8.93%)	5
Back pain [A] †	2/59 (3.39%)	2	1/58 (1.72%)	1	3/56 (5.36%)	3
Bone Pain [A] †	0/59 (0%)	0	0/58 (0%)	0	2/56 (3.57%)	2
Hypercreatinaemia [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Intervertebral disc degeneration [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Musculoskeletal chest pain [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Musculoskeletal pain [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Myalgia [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	2/56 (3.57%)	2
Neck Pain [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0
Pain in the extremity [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Spinal Compression Fracture [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Metastic Neoplasm [E] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Metastic Pain [E] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Tumor associated fever [E] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Nervous system disorders						

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Agitated Depression [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Clonus [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Convulsion [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Dizziness [A] †	1/59 (1.69%)	1	2/58 (3.45%)	2	0/56 (0%)	0
Dysarthria [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Dysgeusia [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Epilepsy [A] †	2/59 (3.39%)	2	0/58 (0%)	0	0/56 (0%)	0
Head Discomfort [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Headache [A] †	1/59 (1.69%)	1	0/58 (0%)	0	5/56 (8.93%)	5
Hypogeusia [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Insomnia [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Loss of consciousness [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Neuralgia [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Neuropathy peripheral [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Paraesthesia [A] †	1/59 (1.69%)	3	0/58 (0%)	0	1/56 (1.79%)	1
Peripheral sensory neuropathy [A] †	0/59 (0%)	0	2/58 (3.45%)	3	0/56 (0%)	0
Somnolence [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0
Syncope [A] †	2/59 (3.39%)	3	0/58 (0%)	0	0/56 (0%)	0
Tremor [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Psychiatric disorders						
Anxiety [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	0/56 (0%)	0

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Depression [F] †	1/59 (1.69%)	2	2/58 (3.45%)	3	2/56 (3.57%)	2
Insomnia [F] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Panic disorder [F] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Sleep disorder due to general medical condition , insomnia type [F] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Renal and urinary disorders						
Bladder hypertrophy [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Dysuria [F] †	0/59 (0%)	0	3/58 (5.17%)	5	0/56 (0%)	0
Haematuria [F] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Hypercreatininaemia [F] †	0/59 (0%)	0	1/58 (1.72%)	1	1/56 (1.79%)	1
Oliguria [F] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Proteinuria [F] †	1/59 (1.69%)	1	3/58 (5.17%)	3	1/56 (1.79%)	5
Renal failure [F] †	2/59 (3.39%)	2	3/58 (5.17%)	4	1/56 (1.79%)	1
Renal failure acute [F] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Strangury [F] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Urinary Tract Infection [F] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Urinary incontinence [F] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Respiratory, thoracic and mediastinal disorders						
Cough [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	2/56 (3.57%)	2
Dysphonia [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Dysponea [A] †	3/59 (5.08%)	3	3/58 (5.17%)	3	4/56 (7.14%)	4
Dysponea exertional [A] †	1/59 (1.69%)	1	2/58 (3.45%)	2	0/56 (0%)	0

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Epistaxis [A] †	0/59 (0%)	0	1/58 (1.72%)	1	1/56 (1.79%)	1
Pulmonary embolism [A] †	1/59 (1.69%)	1	1/58 (1.72%)	1	1/56 (1.79%)	1
Pulmonary hypertension [A] †	0/59 (0%)	0	2/58 (3.45%)	2	0/56 (0%)	0
Skin and subcutaneous tissue disorders						
Acne [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Angioedema [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Dermatitis [A] †	2/59 (3.39%)	8	3/58 (5.17%)	4	0/56 (0%)	0
Dermatitis allergic [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Drug Eruption [A] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Dry Skin [A] †	2/59 (3.39%)	2	0/58 (0%)	0	2/56 (3.57%)	2
Erythema [A] †	5/59 (8.47%)	13	4/58 (6.9%)	4	4/56 (7.14%)	5
Exfoliative rash [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Face Oedema [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Folliculitis [A] †	3/59 (5.08%)	4	1/58 (1.72%)	1	1/56 (1.79%)	1
Onycholysis [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Palmar-plantar erythrodysaesthesia syndrome [A] †	2/59 (3.39%)	2	1/58 (1.72%)	1	0/56 (0%)	0
Pruritus [A] †	1/59 (1.69%)	1	2/58 (3.45%)	2	4/56 (7.14%)	5
Pruritus generalised [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	2
Rash [A] †	15/59 (25.42%)	21	5/58 (8.62%)	5	3/56 (5.36%)	3
Rash erythematous [A] †	2/59 (3.39%)	2	0/58 (0%)	0	0/56 (0%)	0

	Arm A Vandetanib 300 mg		Arm B Vandetanib 100mg + Gemcitab		ARM C Placebo+ Gemcitabine	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Rash maculo-papular [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Skin Toxicity [A] †	2/59 (3.39%)	6	3/58 (5.17%)	3	1/56 (1.79%)	1
Vascular disorders						
Deep Vein thrombosis [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Diastolic hypotension [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Epistaxis [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Essential hypertension [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Haemorrhoids [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	1
Hypertension [A] †	14/59 (23.73%)	17	9/58 (15.52%)	10	4/56 (7.14%)	6
Hypertensive crisis [A] †	1/59 (1.69%)	1	0/58 (0%)	0	1/56 (1.79%)	1
Hypotension [A] †	2/59 (3.39%)	2	1/58 (1.72%)	1	1/56 (1.79%)	1
Phlebitis [A] †	0/59 (0%)	0	0/58 (0%)	0	1/56 (1.79%)	2
Pulmonary embolism [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0
Systolic hypertension [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Venous insufficiency [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Venous thrombosis [A] †	0/59 (0%)	0	1/58 (1.72%)	1	0/56 (0%)	0
Venous thrombosis limb [A] †	1/59 (1.69%)	1	0/58 (0%)	0	0/56 (0%)	0

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.0
B Term from vocabulary, MeDRA 15.0
C Term from vocabulary, MeDra 15.0
D Term from vocabulary, MedDra 15.0
E Term from vocabulary, MedRa 15.0
F Term from vocabulary, Medra 15.0

[1] General disorders and administration site conditions

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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