ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 10/03/2012

ClinicalTrials.gov ID: NCT00306891

Study Identification

Unique Protocol ID:	D8480C00021
Brief Title:	Effect of Food Upon Pharmacokinetics of Single Oral Dose of Cediranib (AZD2171, Recentin™)
Official Title:	Open-label, Randomised, Phase 2 Study in Patients With Advanced Solid Tumours to Determine Effect of Food Upon Pharmacokinetics of a Single Oral Dose of Cediranib (AZD2171, Recentin™), Followed by an Assessment of the Safety & Tolerability of Fixed and Individualised Daily Dosing
Secondary IDs:	2005-003441-13

Study Status

Record Verification:	October 2012
Overall Status:	Completed
Study Start:	June 2006
Primary Completion:	January 2008 [Actual]
Study Completion:	September 2008 [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: 06/Q2404/9 Board Name: Nottingham (2) Regional Ethics Committee Board Affiliation: COREC Phone: 0115 912 3399 Email: linda.ellis@rushcliffe-pct.nhs.uk
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	United Kingdom: Department of Health

Study Description

Brief Summary:	The purpose of this study is to determine whether food has any effect on a single dose of Cediranib (AZD2171, Recentin™)followed by an assessment of the safety and tolerability of fixed daily dosing in comparison to varying dose levels on a patient-by-patient basis.
Detailed Description:	

Conditions

Conditions:	Cancer
Keywords:	Advanced solid tumours Advanced cancer tumor tumour RECENTIN

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Crossover Assignment
Number of Arms:	4

Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Pharmacokinetics Study
Enrollment:	60 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Cediranib 45 mg Fed Part A: Cediranib 45 mg Fed State	Drug: Cediranib 45 mg oral dose Other Names: • RECENTIN™
Experimental: Cediranib 45 mg Fasted Part A: Cediranib 45 mg Fasted State	Drug: Cediranib 45 mg oral dose Other Names: • RECENTIN™
Experimental: Cediranib 45 mg Fixed Dose Part B: Cediranib 45 mg Fixed Dose	Drug: Cediranib 45 mg oral dose Other Names: • RECENTIN™
Experimental: Cediranib 30 - 90 mg Dose Escalation Part B: Cediranib 30 - 90 mg Dose Escalation	Drug: Cediranib 30 - 90 mg oral tablet dose escalation Other Names: • RECENTIN™

Outcome Measures

[See Results Section.]

Eligibility

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

Criteria: Inclusion Criteria:

- Clinical diagnosis of advanced solid tumour.
- Ability to eat a high fat breakfast

Exclusion Criteria:

- Poorly controlled high blood pressure.
- History of significant gastrointestinal problems

Contacts/Locations

Study Officials: AstraZeneca AZD2171 Medical Science Director, MD
Study Director
AstraZeneca

Locations: United Kingdom
Research Site
Manchester, United Kingdom

Research Site
Headington, United Kingdom

Research Site
Glasgow, United Kingdom

Research Site
London, United Kingdom

References

Citations:

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

Study Data/Documents:

Participant Flow

Recruitment Details	This was a two part study.Part A had two arms, fed/fasted and fasted/fed. Part B had two arms, a fixed dose arm and a dose escalation arm.Patients(pts)in Part A were allowed to go in to Part B. Pts who chose not to go in to Part B discontinued the study.Additionally new pts were recruited to Part B. In Parts A/B, there was a total of 60 pts.
Pre-Assignment Details	60 patients were enrolled though only 45 patients were randomized to Part A and 47 to Part B. Completion of Part B means completed at least 16 weeks of treatment.

Reporting Groups

	Description
Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State
Cediranib 45 mg Fixed Dose	Part B: Cediranib 45 mg Fixed Dose
Cediranib 30 to 90 mg Dose Escalation	Part B: Cediranib Dose Escalation

Part A

	Cediranib 45 mg Fed	Cediranib 45 mg Fasted	Cediranib 45 mg Fixed Dose	Cediranib 30 to 90 mg Dose Escalation
Started	23	22	0	0
Completed	18	16	0	0
Not Completed	5	6	0	0
Withdrawal by Subject	1	1	0	0
Condition under investigation worsened	2	2	0	0
Incorrect enrol/entry crit not fulfilled	0	1	0	0
Partial bowel obstruction	1	0	0	0
Reaccumul. of ascites following drainage	0	1	0	0
Suspicion of second malignancy	0	1	0	0
QTC interval outwith elig. criteria	1	0	0	0

Part B

	Cediranib 45 mg Fed	Cediranib 45 mg Fasted	Cediranib 45 mg Fixed Dose	Cediranib 30 to 90 mg Dose Escalation
Started	0	0	16 [1]	31 [2]
Completed	0	0	5	14
Not Completed	0	0	11	17
Death	0	0	1	2
Adverse Event	0	0	5	5
Withdrawal by Subject	0	0	3	1
Condition under investigation worsened	0	0	2	8
Development of study specific disc crit.	0	0	0	1

[1] In Part B: Cediranib 45 mg Fixed Dose 4 new patients were randomized
[2] in Part B: Cediranib Dose Escalation 11 new patients were randomized.

Baseline Characteristics

Reporting Groups

	Description
Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State
Cediranib 45 mg Fixed Dose	Part B: Cediranib 45 mg Fixed Dose
Cediranib 30 to 90 mg Dose Escalation	Part B: Cediranib Dose Escalation

Baseline Measures

	Cediranib 45 mg Fed	Cediranib 45 mg Fasted	Cediranib 45 mg Fixed Dose	Cediranib 30 to 90 mg Dose Escalation	Total
Number of Participants	23	22	16	31	92
Age, Continuous [units: Years] Mean (Standard Deviation)	58.6 (10.6)	51.2 (14.8)	56.4 (13.1)	56.0 (13.5)	56.0 (13.0)

	Cediranib 45 mg Fed	Cediranib 45 mg Fasted	Cediranib 45 mg Fixed Dose	Cediranib 30 to 90 mg Dose Escalation	Total
Gender, Customized [units: participants]					
Female, Part A	10	10	NA [1]	NA [2]	20
Male, Part A	13	12	NA [3]	NA [2]	25
Female, Part B	NA [4]	NA [5]	8	12	20
Male, Part B	NA [6]	NA [5]	8	19	27

[1] Cediranib 45 mg Fixed dose arm existed only in Part B.

[2] Cediranib 30 to 90 mg Dose Escalation existed only in Part B.

[3] Cediranib 45 mg Fixed dose arm existed only in Part B

[4] Cediranib 45 mg Fed/Fasted existed only in Part A.

[5] Cediranib 45 mg Fasted/Fed existed only in Part A.

[6] Cediranib 45 mg Fed/Fasted only in Part A.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Part A: Area Under Plasma Concentration-time Curve (AUC)
Measure Description	Area under plasma concentration-time curve from zero to infinity
Time Frame	Measurements were collected up to 168 hours (following single dosing).
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State

Measured Values

	Cediranib 45 mg Fed	Cediranib 45 mg Fasted
Number of Participants Analyzed	30	32
Part A: Area Under Plasma Concentration-time Curve (AUC) [units: ng*h/mL] Geometric Mean (Full Range)	1920 (778 to 5760)	2392 (604 to 5730)

2. Primary Outcome Measure:

Measure Title	Part A: Maximum Plasma (Peak) Concentration (Cmax)
Measure Description	Maximum plasma drug concentration
Time Frame	Measurements were collected up to 168 hours (following single dosing).
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Arm 1 - Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Arm 2 - Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State

Measured Values

	Arm 1 - Cediranib 45 mg Fed	Arm 2 - Cediranib 45 mg Fasted
Number of Participants Analyzed	31	33
Part A: Maximum Plasma (Peak) Concentration (Cmax) [units: ng/mL] Geometric Mean (Full Range)	87.02 (27.6 to 265)	127.9 (35.6 to 334)

3. Secondary Outcome Measure:

Measure Title	Part A: AUC (0-t)
Measure Description	Area under the curve from time 0 to the last measureable time point
Time Frame	Measurements were collected up to 168 hours (following single dosing).
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Arm 1 - Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Arm 2 - Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State

Measured Values

	Arm 1 - Cediranib 45 mg Fed	Arm 2 - Cediranib 45 mg Fasted
Number of Participants Analyzed	30	32
Part A: AUC (0-t) [units: ng*h/mL] Geometric Mean (Full Range)	1896 (764 to 5700)	2348 (599 to 5290)

4. Secondary Outcome Measure:

Measure Title	Part A: Time to Peak or Maximum Concentration (Tmax)
Measure Description	Time to reach peak or maximum concentration or maximum response
Time Frame	Measurements were collected up to 168 hours (following single dosing).
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Arm 1 - Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Arm 2 - Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State

Measured Values

	Arm 1 - Cediranib 45 mg Fed	Arm 2 - Cediranib 45 mg Fasted
Number of Participants Analyzed	31	33
Part A: Time to Peak or Maximum Concentration (Tmax) [units: hr] Geometric Mean (Full Range)	4.59 (2.0 to 25)	3.52 (2.0 to 6.1)

5. Secondary Outcome Measure:

Measure Title	Part A: Terminal Phase Half-life (t1/2λz)
Measure Description	Terminal phase half-life
Time Frame	Measurements were collected up to 168 hours (following single dosing).
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Arm 1 - Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Arm 2 - Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State

Measured Values

	Arm 1 - Cediranib 45 mg Fed	Arm 2 - Cediranib 45 mg Fasted
Number of Participants Analyzed	30	32
Part A: Terminal Phase Half-life (t1/2λz) [units: hr]	23.99 (12.1 to 37.5)	24.72 (10.2 to 60.2)

	Arm 1 - Cediranib 45 mg Fed	Arm 2 - Cediranib 45 mg Fasted
Geometric Mean (Full Range)		

6. Secondary Outcome Measure:

Measure Title	Part A: Apparent Total Body Clearance (CL/F)
Measure Description	Apparent total body clearance of drug from plasma
Time Frame	Measurements were collected up to 168 hours (following single dosing).
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Arm 1 - Cediranib 45 mg Fed	Part A: Cediranib 45 mg Fed State
Arm 2 - Cediranib 45 mg Fasted	Part A: Cediranib 45 mg Fasted State

Measured Values

	Arm 1 - Cediranib 45 mg Fed	Arm 2 - Cediranib 45 mg Fasted
Number of Participants Analyzed	30	32
Part A: Apparent Total Body Clearance (CL/F) [units: L/h] Geometric Mean (Full Range)	23.44 (7.81 to 57.8)	18.81 (7.85 to 74.5)

7. Secondary Outcome Measure:

Measure Title	Part B: Best Overall Response Rate (ORR)

Measure Description	Evaluation of target lesions Complete Response(CR)Disappearance of all target lesions Partial Response(PR) At least a 30% decrease in the sum of LD(longest diameter)of target lesions taking as reference the baseline sum LD.Progressive Disease(PD).At least a 20% increase in the sum of LD of target lesions taking as references the smallest sum LD recorded(either at baseline or at previous assessment since treatment began).Stable Disease(SD) Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.Note: Appearance of new lesions only counts towards the overall visit response,not towards the response of target or non-target lesions. Evaluation of non-target lesions Complete Response(CR)Disappearance of all non-target lesions Non-Complete Response(non-CR/Non-Progression[non-PD])Persistence of one or more non-target lesion or/and maintenance of tumour marker level above the normal limits.Progression(PD)Unequivocal progression of existing non-target lesions
Time Frame	Baseline, week 8, week 16 and every 8 weeks thereafter until discontinuation.
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description

ITT (intention-to-treat) patients with baseline RECIST data

Reporting Groups

	Description
Arm 3 - Cediranib 45 mg Fixed Dose	Part B: Cediranib 45 mg Fixed Dose
Arm 4 - Cediranib 30-90 mg Dose Escalation	Part B: Cediranib 30-90 mg Dose Escalation

Measured Values

	Arm 3 - Cediranib 45 mg Fixed Dose	Arm 4 - Cediranib 30-90 mg Dose Escalation
Number of Participants Analyzed	15	29
Part B: Best Overall Response Rate (ORR) [units: Participants]	1	3

8. Secondary Outcome Measure:

Measure Title	Part B: Progression-free Survival (PFS)

Measure Description	Target lesions: Progressive Disease (PD) At least a 20% increase in the sum of LD (longest diameter)of target lesions taking as references the smallest sum LD recorded (either at baseline or at previous assessment since treatment began). Non target lesions: Persistence of one or more non-target lesion or/and maintenance of tumour marker level above the normal limits. Progression (PD) Unequivocal progression of existing non-target lesions.
Time Frame	Number of days from randomisation until progressive disease based on RECIST (progression of target lesions, clear progression of existing non-target lesions or the appearance of one or more new lesions) or death in the absence of progression.
Safety Issue?	No
Anticipated Reporting Date	April 2012

Analysis Population Description

ITT (intention-to-treat) patients with baseline RECIST data.One patient was randomized and had baseline RECIST assessments, but did not have any further RECIST assessments. Therefore they were censored at baseline, meaning the lowest value in the range was set to zero.

Reporting Groups

	Description
Arm 3 - Cediranib 45 mg Fixed Dose	Part B: Cediranib 45 mg Fixed Dose
Arm 4 - Cediranib 30-90 mg Dose Escalation	Part B: Cediranib 30-90 mg Dose Escalation

Measured Values

	Arm 3 - Cediranib 45 mg Fixed Dose	Arm 4 - Cediranib 30-90 mg Dose Escalation
Number of Participants Analyzed	15	29
Part B: Progression-free Survival (PFS) [units: Days] Median (Full Range)	135 (39 to 314)	139 (0 to 454)

Reported Adverse Events

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

Reporting Groups

	Description
Cediranib 45 mg Part A	Part A: Cediranib 45 mg
Cediranib 45 mg Fixed Dose	Part B: Cediranib 45 mg Fixed Dose
Cediranib 30 - 90 mg Dose Escalation	Cediranib 30 - 90 mg Dose Escalation

Serious Adverse Events

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	6/39 (15.38%)	9/16 (56.25%)	20/31 (64.52%)
Cardiac disorders			
Angina Pectoris [A] †	1/39 (2.56%)	1/16 (6.25%)	0/31 (0%)
Cardiac Failure [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Gastrointestinal disorders			
Abdominal Pain [A] †	0/39 (0%)	2/16 (12.5%)	3/31 (9.68%)
Abdominal Pain Lower [A] †	1/39 (2.56%)	0/16 (0%)	0/31 (0%)
Constipation [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Diarrhoea [A] †	0/39 (0%)	1/16 (6.25%)	3/31 (9.68%)
Duodenitis [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Enteritis [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Gastric Perforation [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Gastric Ulcer [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Gastrointestinal Haemorrhage [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Gastrointestinal Perforation [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Intestinal Perforation [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Large Intestine Perforation [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Vomiting [A] †	0/39 (0%)	0/16 (0%)	3/31 (9.68%)
General disorders			
Non-Cardiac Chest Pain [A] †	1/39 (2.56%)	0/16 (0%)	0/31 (0%)
Pain [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Pyrexia [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Hepatobiliary disorders			
Bile Duct Obstruction [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Jaundice Cholestatic [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Infections and infestations			
Central Line Infection [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Clostridial Infection [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Sepsis [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Urinary Tract Infection [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Viral Labyrinthitis [A] †	1/39 (2.56%)	0/16 (0%)	0/31 (0%)
Injury, poisoning and procedural complications			
Tracheostomy Malfunction [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Metabolism and nutrition disorders			
Dehydration [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Hypercalcaemia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Musculoskeletal and connective tissue disorders			
Arthralgia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pathological Fracture [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intracranial Tumour Haemorrhage [A] †	1/39 (2.56%)	0/16 (0%)	0/31 (0%)
Nervous system disorders			
Spinal Cord Compression [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Psychiatric disorders			
Suicide Attempt [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Renal and urinary disorders			
Renal Disorder [A] †	1/39 (2.56%)	0/16 (0%)	0/31 (0%)
Urinary Retention [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Respiratory, thoracic and mediastinal disorders			
Hydropneumothorax [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Pleural Effusion [A] †	1/39 (2.56%)	0/16 (0%)	0/31 (0%)
Pulmonary Embolism [A] †	0/39 (0%)	0/16 (0%)	1/31 (3.23%)
Vascular disorders			
Hypertension [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)

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

Other Adverse Events

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

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	34/39 (87.18%)	16/16 (100%)	31/31 (100%)
Blood and lymphatic system disorders			
Anaemia [A] †	0/39 (0%)	2/16 (12.5%)	1/31 (3.23%)
Haemoglobinaemia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Lymphadenopathy [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Thrombocytopenia [A] †	0/39 (0%)	2/16 (12.5%)	3/31 (9.68%)
Cardiac disorders			
Bradycardia [A] †	2/39 (5.13%)	0/16 (0%)	1/31 (3.23%)
Bundle Branch Block Right [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Ear and labyrinth disorders			
Deafness Unilateral [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Endocrine disorders			
Hypothyroidism [A] †	0/39 (0%)	1/16 (6.25%)	4/31 (12.9%)
Eye disorders			
Dry Eye [A] †	0/39 (0%)	2/16 (12.5%)	0/31 (0%)
Visual Disturbance [A] †	0/39 (0%)	0/16 (0%)	2/31 (6.45%)
Gastrointestinal disorders			
Abdominal Pain [A] †	1/39 (2.56%)	4/16 (25%)	9/31 (29.03%)
Abdominal Pain Upper [A] †	1/39 (2.56%)	1/16 (6.25%)	1/31 (3.23%)
Constipation [A] †	4/39 (10.26%)	10/16 (62.5%)	10/31 (32.26%)
Diarrhoea [A] †	5/39 (12.82%)	13/16 (81.25%)	25/31 (80.65%)

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Dry Mouth [A] †	1/39 (2.56%)	1/16 (6.25%)	4/31 (12.9%)
Dyspepsia [A] †	0/39 (0%)	3/16 (18.75%)	3/31 (9.68%)
Epigastric Discomfort [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Gastrooesophageal Reflux Disease [A] †	2/39 (5.13%)	0/16 (0%)	0/31 (0%)
Lip Blister [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Mouth Ulceration [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Nausea [A] †	9/39 (23.08%)	11/16 (68.75%)	17/31 (54.84%)
Oral Pain [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Stomatitis [A] †	0/39 (0%)	4/16 (25%)	9/31 (29.03%)
Tongue Ulceration [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Vomiting [A] †	4/39 (10.26%)	10/16 (62.5%)	14/31 (45.16%)
General disorders			
Fatigue [A] †	8/39 (20.51%)	5/16 (31.25%)	10/31 (32.26%)
Malaise [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Oedema Peripheral [A] †	2/39 (5.13%)	1/16 (6.25%)	4/31 (12.9%)
Pyrexia [A] †	0/39 (0%)	0/16 (0%)	2/31 (6.45%)
Unevaluable Event [A] †	0/39 (0%)	0/16 (0%)	2/31 (6.45%)
Infections and infestations			
Lower Respiratory Tract Infection [A] †	0/39 (0%)	1/16 (6.25%)	2/31 (6.45%)
Neutropenic Sepsis [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Oral Candidiasis [A] †	1/39 (2.56%)	1/16 (6.25%)	3/31 (9.68%)
Pneumonia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Postoperative Wound Infection [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Rhinitis [A] †	0/39 (0%)	2/16 (12.5%)	1/31 (3.23%)
Tooth Abscess [A] †	0/39 (0%)	2/16 (12.5%)	1/31 (3.23%)
Urinary Tract Infection [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Vaginal Candidiasis [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Viral Infection [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Injury, poisoning and procedural complications			
Contusion [A] †	1/39 (2.56%)	0/16 (0%)	2/31 (6.45%)
Investigations			
Alanine Aminotransferase Increased [A] †	0/39 (0%)	1/16 (6.25%)	2/31 (6.45%)
Aspartate Aminotransferase Increased [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Blood Pressure Increased [A] †	2/39 (5.13%)	0/16 (0%)	0/31 (0%)
Blood Thyroid Stimulating Hormone Increased [A] †	0/39 (0%)	2/16 (12.5%)	7/31 (22.58%)
Liver Function Test Abnormal [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Weight Decreased [A] †	1/39 (2.56%)	2/16 (12.5%)	8/31 (25.81%)
Metabolism and nutrition disorders			
Alkalosis [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Anorexia [A] †	3/39 (7.69%)	3/16 (18.75%)	6/31 (19.35%)
Decreased Appetite [A] †	2/39 (5.13%)	4/16 (25%)	8/31 (25.81%)
Hyperglycaemia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Hypokalaemia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Metabolic Acidosis [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Musculoskeletal and connective tissue disorders			
Arthralgia [A] †	1/39 (2.56%)	2/16 (12.5%)	4/31 (12.9%)
Back Pain [A] †	1/39 (2.56%)	1/16 (6.25%)	6/31 (19.35%)
Flank Pain [A] †	0/39 (0%)	0/16 (0%)	2/31 (6.45%)
Groin Pain [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Joint Swelling [A] †	0/39 (0%)	0/16 (0%)	3/31 (9.68%)
Mobility Decreased [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Muscle Spasms [A] †	1/39 (2.56%)	1/16 (6.25%)	1/31 (3.23%)
Musculoskeletal Chest Pain [A] †	1/39 (2.56%)	1/16 (6.25%)	0/31 (0%)
Musculoskeletal Pain [A] †	0/39 (0%)	0/16 (0%)	3/31 (9.68%)
Myalgia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Myopathy [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Pain In Extremity [A] †	1/39 (2.56%)	0/16 (0%)	2/31 (6.45%)
Nervous system disorders			
Dizziness [A] †	2/39 (5.13%)	1/16 (6.25%)	6/31 (19.35%)
Dysgeusia [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)
Headache [A] †	2/39 (5.13%)	5/16 (31.25%)	5/31 (16.13%)
Lethargy [A] †	8/39 (20.51%)	4/16 (25%)	7/31 (22.58%)
Neuralgia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Sciatica [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Tremor [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Psychiatric disorders			
Anxiety [A] †	2/39 (5.13%)	1/16 (6.25%)	0/31 (0%)
Depressed Mood [A] †	2/39 (5.13%)	0/16 (0%)	0/31 (0%)
Depression [A] †	0/39 (0%)	1/16 (6.25%)	3/31 (9.68%)
Insomnia [A] †	1/39 (2.56%)	1/16 (6.25%)	0/31 (0%)
Renal and urinary disorders			
Proteinuria [A] †	0/39 (0%)	1/16 (6.25%)	2/31 (6.45%)
Urinary Tract Disorder [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Urine Odour Abnormal [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Reproductive system and breast disorders			
Amenorrhoea [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Menorrhagia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Respiratory, thoracic and mediastinal disorders			
Cough [A] †	1/39 (2.56%)	2/16 (12.5%)	1/31 (3.23%)
Dysphonia [A] †	2/39 (5.13%)	4/16 (25%)	7/31 (22.58%)
Dyspnoea [A] †	1/39 (2.56%)	2/16 (12.5%)	3/31 (9.68%)
Dyspnoea Exertional [A] †	0/39 (0%)	0/16 (0%)	2/31 (6.45%)
Hiccups [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Hydropneumothorax [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Pharyngolaryngeal Pain [A] †	0/39 (0%)	3/16 (18.75%)	0/31 (0%)
Productive Cough [A] †	0/39 (0%)	2/16 (12.5%)	0/31 (0%)
Skin and subcutaneous tissue disorders			

	Cediranib 45 mg Part A	Cediranib 45 mg Fixed Dose	Cediranib 30 - 90 mg Dose Escalation
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Alopecia [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Dry Skin [A] †	0/39 (0%)	3/16 (18.75%)	1/31 (3.23%)
Hyperhidrosis [A] †	0/39 (0%)	0/16 (0%)	2/31 (6.45%)
Skin Hyperpigmentation [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Skin Induration [A] †	0/39 (0%)	0/16 (0%)	2/31 (6.45%)
Skin Lesion [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Vascular disorders			
Hypertension [A] †	9/39 (23.08%)	10/16 (62.5%)	23/31 (74.19%)
Hypotension [A] †	0/39 (0%)	1/16 (6.25%)	0/31 (0%)
Lymphoedema [A] †	0/39 (0%)	1/16 (6.25%)	1/31 (3.23%)

† Indicates events were collected by systematic assessment.
A 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.

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.

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