ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 04/11/2013

ClinicalTrials.gov ID: NCT00350727

Study Identification

Unique Protocol ID:	VEG102857
Brief Title:	Pazopanib In Combination With Lapatinib In Adult Patients With Relapsed Malignant Glioma (VEG102857)
Official Title:	Phase I and II, Open-Label, Multi-Center Trials of Pazopanib in Combination With Lapatinib in Adult Patients With Relapsed Malignant Glioma
Secondary IDs:	

Study Status

Record Verification:	May 2012
Overall Status:	Completed
Study Start:	December 2006
Primary Completion:	December 2009 [Actual]
Study Completion:	December 2009 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? No

	Delayed Posting?
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 65,747 Serial Number: 0168 Has Expanded Access? No
Review Board:	Approval Status: Approved Approval Number: 14 Dec 2006 Board Name: University of Texas MD Anderson Cancer Center Institutional Review Board Board Affiliation: University of Texas MD Anderson Cancer Center Institutional Review Board Phone: Email: martin.c.curtis@gsk.com
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	European Union: European Medicines Agency United States: Food and Drug Administration

Study Description

Brief Summary:	This study is being conducted to characterize the safety/tolerability of pazopanib and lapatinib when administered in combination with enzyme-inducing anticonvulsants in patients with recurrent Grade III or IV malignant gliomas.
Detailed Description:	This study is being conducted to characterize the safety/tolerability of pazopanib and lapatinib when administered in combination with enzyme-inducing anticonvulsants in patients with recurrent Grade III or IV malignant gliomas.

Conditions

Conditions:	Glioma
Keywords:	relapsed lapatinib Pazopanib glioblastoma

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2

Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Pharmacokinetics Study
Enrollment:	75 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Combination Pazopanib and Lapatinib in combination. Subjects remain on treatment until disease progression or withdrawal from study.	Drug: pazopanib Pazopanib is a novel compound being developed for the treatment of various cancers. Drug: lapatinib Lapatinib is a novel compound being developed for the treatment of various cancers. Other Names: • lapatinib • pazopanib

Outcome Measures

[See Results Section.]

Eligibility

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

Phase I

- Patients are on EIAC for a minimum of 15 days. Patients may be on more than one anti-convulsant (AC). At least one of the ACs must be an EIAC.

- Patients with anaplastic astrocytoma, anaplastic oligodendroglioma, mixed anaplastic oligoastrocytoma, glioblastoma multiforme, or gliosarcoma at recurrence
- Patients whose diagnostic pathology confirmed these pathologies will not need re-biopsy
- Patients with prior low-grade glioma are eligible if histologic assessment demonstrates transformation to Grade III or IV malignant glioma Phase II
- Patients must have histologically confirmed glioblastoma multiforme or gliosarcoma in first or second recurrence.
- Patients may not have received more than two prior cytotoxic chemotherapy containing regimen.
- Patients must not have received prior treatment with VEGFR, ErbB1, ErbB2 inhibitors including but not limited to PTK-787, Sorafenib, Sutent, Tarceva, Iressa, Erbitux, and Herceptin. Prior Avastin therapy is permitted provided three months has elapsed before Day 1, Treatment Period 1.
- Tumor tissue must be analyzed for PTEN and epidermal growth factor receptor (EGFR) vIII prior to dosing.
- Patients with prior low-grade glioma are eligible if histologic assessment demonstrates transformation to Grade IV malignant glioma.
- Patients must not be on an EIAC. NOTE: Once the (optimally tolerated regimen) OTR in Phase I is determined and all patients in the expanded cohort have completed 1 treatment period then patients on EIAC may be enrolled in the Phase II component of the study.

Phase I and II

- Male or female, age at least 18 years of age.
- Eastern Cooperative Oncology Group (ECOG) status 0 to 1 as per protocol.
- Clinical lab results as per protocol
- Has a left ventricular ejection fraction (LVEF) at least 50% based on echocardiogram (ECHO) or Multi Gated Aquisition (MUGA) or within the institutional normal range.
- Adequate renal function
- Creatinine clearance more than 50 mL/min as calculated by the Cockcroft-Gault formula as per protocol.
- Urine Protein Creatinine (UPC) ratio of less than or equal to 1 as per protocol.
- Able to swallow and retain oral medications.
- A woman is eligible to enter and participate in the study if she is of:

  - Non-childbearing potential (i.e., physiologically incapable of becoming pregnant), including any female who:
- Has had a hysterectomy,
- Has had a bilateral oophorectomy (ovariectomy),
- Has had a bilateral tubal ligation,
- Is post-menopausal (total cessation of menses for at least 1 year)

  - Childbearing potential, has a negative serum pregnancy test at screening, and agrees to use adequate contraception. Acceptable contraceptive methods, when used consistently and in accordance with both the product label and the instructions of the physician, are as follows:
- An intrauterine device (IUD) with a documented failure rate of less than 1% per year.
- Vasectomized partner who is sterile prior to the female patient's entry and is the sole sexual partner for that female.
- Double-barrier contraception (condom with spermicidal jelly, foam suppository, or film; diaphragm with spermicide; or male condom and diaphragm with spermicide).
- A man with a female partner of childbearing potential is eligible to enter and participate in the study if he uses a barrier method of contraception or abstinence during the study.

- If sexually active, patients will continue the recommended contraceptive measures for the duration of the treatments and for 28 days following discontinuation of therapy.
- Signed informed consent approved by the Institutional Review Board prior to patient entry.

Exclusion criteria:

- Poorly controlled hypertension as per protocol. NOTE: Initiation or adjustment of BP medication is permitted prior to study entry provided that patient has two consecutive BP readings less than 140/90 mmHg each separated by a minimum of 24 hrs. These readings need to be collected prior to enrolment.
- Concurrent severe and/or uncontrolled medical disease (e.g. uncontrolled diabetes, congestive cardiac failure, poorly controlled hypertension, history of labile hypertension, history of poor compliance with antihypertensive regimen, chronic renal disease, or active uncontrolled infection) that could compromise participation in the study.
- History of myocardial infarction, admission for unstable angina, cardiac angioplasty or stenting within three months of Day 1, Treatment Period 1.
- Has Class III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system as per protocol.
- QTc prolongation defined as a corrected QT (QTc) interval greater than or equal to 470 milliseconds.
- History of venous or arterial thrombosis within 3 months of Day 1, Treatment Period 1.
- Current use of therapeutic warfarin. NOTE: both low molecular weight heparin and prophylactic low-dose warfarin are permitted; however, prothrombin time/partial thromboplastin time (PT/PTT) must meet above inclusion criteria.
- Excessive risk of bleeding as defined by stroke within the prior 6 months, history of central nervous system (CNS) or intraocular bleed, or septic endocarditis.
- Evidence of intratumor hemorrhage on pretreatment diagnostic imaging, except for stable post-operative Grade 1 hemorrhage.
- Active systemic bleeding, such as gastrointestinal bleeding or gross hematuria.
- Female patients who are pregnant or breast feeding.
- Acute or chronic liver disease (i.e., hepatitis, cirrhosis).
- Patients who received investigational drugs less than 21days prior to Day 1, Treatment Period 1, or who have not recovered from the toxic effects of such therapy.
- Patients who received chemotherapy less than or equal to 21days prior (6 weeks for prior nitrosourea or mitomycin C) to Day 1, Treatment Period 1, or who have not recovered from the toxic effects of such therapy.
- Patients who received radiation therapy less than or equal to 12 weeks prior to Day 1, Treatment Period 1, or who have not recovered from the toxic effects of such therapy as per protocol.
- Patients who received biologic, immunotherapeutic or cytostatic agents less than or equal to 14 days prior to Day 1, Treatment Period 1, or who have not recovered from the toxic effects of such therapy.
- Patient is less than 3 years free of another primary malignancy except: if the other primary malignancy is not currently clinically significant or requiring active intervention. Patients with a history of completely resected non-melanoma skin cancer or successfully treated in situ carcinoma are eligible.
- Surgical resection of brain tumor or any other surgery less than or equal to 21 days prior to Day 1, Treatment Period 1, or who have not recovered from side effects of such a procedure. Patients who undergo stereotactic biopsy less than or equal to 14 days prior to Day 1 of Treatment Period 1, or who have not recovered from side effects of such a procedure.
- Patients with any Grade of intraparenchymal CNS hemorrhage. Exceptions include Grade 1 intraparenchymal hemorrhage in the immediate post-operative period, or Grade 1 intraparenchymal hemorrhage that has been stable for at least 3 months.
- Patients unwilling to or unable to comply with the protocol.
- Any serious and/or unstable pre-existing medical, psychiatric, or other condition (including lab abnormalities) that could interfere with patient safety or obtaining informed consent.

- History of malabsorption syndrome, disease significantly affecting gastrointestinal function or major resection of the stomach or small bowel that could affect absorption, distribution, metabolism or excretion of study drugs. Has any unresolved bowel obstruction or diarrhea.
- Psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol.
- Is on any specifically prohibited medication or requires any of these medications during treatment.

Contacts/Locations

Study Officials: GSK Clinical Trials
Study Director
GlaxoSmithKline

Locations:

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	Phase I and Phase II had two separate participant populations. Enrollment in Phase II was not dependent on the number of participants completing Phase I.

Reporting Groups

	Description
Phase I: Pazopanib 200-800 mg/ Lapatinib 500-1500 mg	Starting dose of oral pazopanib of 200 milligrams (mg) once daily (OD) and oral lapatinib 1500 mg OD. The dose of pazopanib (200-800 mg) and lapatinib (500-1500 mg) in cohorts enrolled subsequent to the first dose cohort was determined by the toxicity profile of the combination therapy and the pharmacokinetic results from the prior cohort.
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).

	Description
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Phase I: Dose Escalation

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Started	34	0	0
Completed	0	0	0
Not Completed	34	0	0
Adverse Event	4	0	0
Lack of Efficacy	25	0	0
Death	1	0	0
Physician Decision	1	0	0
Transition to Extension Phase	3	0	0

Phase II

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Started	0	19	22
Completed	0	0	0
Not Completed	0	19	22
Disease Progression	0	15	16
Clinical Deterioration	0	1	0
Withdrawal by Subject	0	2	1
Adverse Event	0	1	1
Death	0	0	2
Sponsor Terminated Study	0	0	1
Enrolled in Rollover Study	0	0	1

Baseline Characteristics

Reporting Groups

	Description
Phase I: Pazopanib 200-800 mg/ Lapatinib 500-1500 mg	Starting dose of oral pazopanib of 200 milligrams (mg) once daily (OD) and oral lapatinib 1500 mg OD. The dose of pazopanib (200-800 mg) and lapatinib (500-1500 mg) in cohorts enrolled subsequent to the first dose cohort was determined by the toxicity profile of the combination therapy and the pharmacokinetic results from the prior cohort.
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Baseline Measures

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative	Total
Number of Participants	34	19	22	75
Age, Customized [1] [units: participants]				
20-29 years old	1	0	2	3
30-39 years old	8	0	3	11
40-49 years old	11	6	6	23
50-59 years old	10	5	8	23
60-69 years old	3	7	2	12
>=70 years old	1	1	1	3
Gender, Male/Female [units: participants]				
Female	11	5	5	21
Male	23	14	17	54
Race/Ethnicity, Customized [units: participants]				
African American/African Heritage	0	0	1	1

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative	Total
White/Caucasian/European Heritage	34	19	21	74

[1] Number of participants falling into the indicated age groups.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With the Indicated Change From Baseline to Study Completion in Systolic Blood Pressure
Measure Description	Each on-study and follow-up laboratory parameter and vital sign was compared to the participant's baseline (BL) values to investigate what changes occurred. mmHg, millimeters of mercury.
Time Frame	Baseline to study completion (up to 844 days for Phase I, up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population (all participants who were given any dose of study medication) for Phases I and II. One participant withdrew in Phase I due to death; change from baseline was not calculated for this participant.

Reporting Groups

	Description
Phase I: Pazopanib 200-800 mg/ Lapatinib 500-1500 mg	Starting dose of oral pazopanib of 200 milligrams (mg) once daily (OD) and oral lapatinib 1500 mg OD. The dose of pazopanib (200-800 mg) and lapatinib (500-1500 mg) in cohorts enrolled subsequent to the first dose cohort was determined by the toxicity profile of the combination therapy and the pharmacokinetic results from the prior cohort.
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	33	19	22

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants With the Indicated Change From Baseline to Study Completion in Systolic Blood Pressure [units: participants]			
BL, 90-<140 mmHg; shift to post-BL, 90-<140 mmgHg	21	12	11
BL, 90-<140 mmHg; shift to post-BL, 140-<170 mmHg	12	3	8
BL, 90-<140 mmHg; shift to post-BL, >=170 mmHg	0	0	1
BL, 140-<170 mmHg; shift to post-BL, 90-<140 mmHg	0	1	0
BL, 140-<170 mmHg; shift to post-BL, 140-<170 mmHg	0	2	1
BL, 140-<170 mmHg; shift to post-BL, >=170 mmHg	0	0	0
BL, >=170 mmHg; shift to post-BL, 140-<170 mmHg	0	1	1

2. Primary Outcome Measure:

Measure Title	Number of Participants With the Indicated Change From Baseline to Study Completion in Diastolic Blood Pressure
Measure Description	Each on-study and follow-up laboratory parameter and vital sign was compared to the participant's baseline (BL) values to investigate what changes occurred. mmHg, millimeters of mercury.
Time Frame	Baseline to study completion (up to 844 days for Phase I, up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phases I and II. One participant withdrew in Phase I due to death; change from baseline was not calculated for this participant.

Reporting Groups

	Description
Phase I: Pazopanib 200-800 mg/ Lapatinib 500-1500 mg	Starting dose of oral pazopanib of 200 milligrams (mg) once daily (OD) and oral lapatinib 1500 mg OD. The dose of pazopanib (200-800 mg) and lapatinib (500-1500 mg) in cohorts enrolled subsequent to the first dose cohort was determined by the toxicity profile of the combination therapy and the pharmacokinetic results from the prior cohort.
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	33	19	22
Number of Participants With the Indicated Change From Baseline to Study Completion in Diastolic Blood Pressure [units: participants]			
BL, 50-<90 mmHg; shift to post-BL, 50-<90 mmHg	23	13	9
BL, 50-<90 mmHg; shift to post-BL, 90-<110 mmHg	9	4	10
BL, 90-<110 mmHg; shift to post-BL, 50-<90 mmHg	0	1	0
BL, 90-<110 mmHg; shift to post-BL, 90-<110 mmHg	1	0	2
BL, 90-<110 mmHg; shift to post-BL, >=110 mmHg	0	1	1

3. Primary Outcome Measure:

Measure Title	Number of Participants With the Indicated Change From Baseline to Study Completion in Heart Rate
Measure Description	Each on-study and follow-up laboratory parameter and vital sign was compared to the participant's baseline (BL) values to investigate what changes occurred. bpm, beats per minute.
Time Frame	Baseline to study completion (up to 844 days for Phase I, up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phases I and II. One participant withdrew in Phase I due to death; change from baseline was not calculated for this participant.

Reporting Groups

	Description
Phase I: Pazopanib 200-800 mg/ Lapatinib 500-1500 mg	Starting dose of oral pazopanib of 200 milligrams (mg) once daily (OD) and oral lapatinib 1500 mg OD. The dose of pazopanib (200-800 mg) and lapatinib (500-1500 mg) in cohorts enrolled subsequent to the first dose cohort was determined by the toxicity profile of the combination therapy and the pharmacokinetic results from the prior cohort.
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	33	19	22
Number of Participants With the Indicated Change From Baseline to Study Completion in Heart Rate [units: participants]			
BL, 44-100 bpm; shift to post-BL, 44-100 bpm	31	14	19
BL, 44-100 bpm; shift to post-BL, 101-120 bpm	0	3	2
BL, 101-120 bpm; shift to post-BL, 101-120 bpm	2	0	0
BL, 101-120 bpm; shift to post-BL, >120 bpm	0	1	0
BL, >120 bpm; shift to post-BL, 44-100 bpm	0	0	1
BL, missing; shift to post-BL, 44-100 bpm	0	1	0

4. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Albumin
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.

Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	21
Mean Change From Baseline to Maximum Value in Phase II of the Study for Albumin [units: grams per liter (g/L)] Mean (Standard Deviation)	-5.9 (9.57)	-6.7 (9.95)

5. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Alkaline Phosphatase, Alanine Aminotransferase, Aspartate Aminotransferase, and Lactate Dehydrogenase
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Mean Change From Baseline to Maximum Value in Phase II of the Study for Alkaline Phosphatase, Alanine Aminotransferase, Aspartate Aminotransferase, and Lactate Dehydrogenase [units: International Units per Liter (IU/L)] Mean (Standard Deviation)		
Alkaline phosphatase, n=19, 21	18.6 (54.02)	33.9 (109.99)
Alanine aminotransferase, n=19, 22	56.1 (131.99)	132.7 (393.89)
Aspartate aminotransferase, n=19, 22	36.4 (88.50)	52.7 (178.02)
Lactate dehydrogenase, n=18, 19	291.50 (443.725)	171.63 (606.986)

6. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Amylase and Lipase
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	19
Mean Change From Baseline to Maximum Value in Phase II of the Study for Amylase and Lipase [units: Units per liter (U/L)] Mean (Standard Deviation)		
Amylase	22.72 (28.060)	20.05 (30.288)
Lipase	131.4 (318.13)	120.5 (163.51)

7. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Total Bilirubin and Creatinine
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	21
Mean Change From Baseline to Maximum Value in Phase II of the Study for Total Bilirubin and Creatinine [units: micromoles per liter (µmol/l)] Mean (Standard Deviation)		
Total bilirubin	6.174 (7.2714)	23.562 (71.1671)
Creatinine	6.93 (10.444)	9.59 (14.852)

8. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Calcium, Glucose, Potassium, Magnesium, Inorganic Phosphorus, Sodium, and Urea
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	21

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Mean Change From Baseline to Maximum Value in Phase II of the Study for Calcium, Glucose, Potassium, Magnesium, Inorganic Phosphorus, Sodium, and Urea [units: millimoles per liter (mmol/l)] Mean (Standard Deviation)		
Calcium, n=19, 21	0.004 (0.1257)	0.019 (0.0952)
Glucose, n=19, 21	0.082 (4.1342)	1.850 (2.7180)
Potassium, n=19, 21	0.17 (0.471)	0.30 (0.264)
Magnesium, n=19, 19	0.022 (0.0676)	0.040 (0.0853)
Sodium, n=19, 21	1.7 (2.96)	1.3 (1.85)
Urea, n=19, 21	0.770 (1.6840)	1.071 (2.1736)
Inorganic phosphorus, n=19, 20	0.090 (0.2352)	0.076 (0.2048)

9. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Thyroxine and Free T3 (Triiodothyronine)
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	16	13
Mean Change From Baseline to Maximum Value in Phase II of the Study for Thyroxine and Free T3 (Triiodothyronine) [units: picomoles per liter (pmol/l)] Mean (Standard Deviation)		
Thyroxine, n=16, 13	-8.052 (30.2175)	10.806 (40.5626)
Free T3, n=4, 4	0.420 (0.5010)	-2.442 (2.3525)

10. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Thyroid Stimulating Hormone
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	18	20
Mean Change From Baseline to Maximum Value in Phase II of the Study for Thyroid Stimulating Hormone [units: milliunits per liter (mU/L)]	1.37 (2.106)	2.59 (4.377)

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Mean (Standard Deviation)		

11. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Total T3
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	13	8
Mean Change From Baseline to Maximum Value in Phase II of the Study for Total T3 [units: nanomoles per liter (nmol/l)] Mean (Standard Deviation)	-0.181 (0.6521)	-0.104 (0.3516)

12. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Hemoglobin
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)

Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Mean Change From Baseline to Maximum Value in Phase II of the Study for Hemoglobin [units: grams per liter (g/L)] Mean (Standard Deviation)	-4.6 (11.25)	-8.0 (16.75)

13. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Hematocrit
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline. The hematocrit is the proportion of blood volume that is occupied by red blood cells.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Mean Change From Baseline to Maximum Value in Phase II of the Study for Hematocrit [units: percent] Mean (Standard Deviation)	-0.016 (0.0320)	-0.027 (0.0452)

14. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Lymphocytes, Neutrophils, Platelet Count, and White Blood Count
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Mean Change From Baseline to Maximum Value in Phase II of the Study for Lymphocytes, Neutrophils, Platelet Count, and White Blood Count [units: giga (10^9) per liter (GI/L)] Mean (Standard Deviation)		
Lymphocytes, n=16, 19	-0.26 (0.556)	-0.21 (0.573)
Total Neutrophils, n=16, 18	-2.87 (3.021)	-4.72 (5.067)
Platelet count, n=19, 22	-58.7 (53.98)	-55.7 (59.79)
White blood cells, n=19, 22	-2.63 (2.934)	-4.06 (6.026)

15. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for International Normalized Ratio (Prothrombin Time)
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline. Prothrombin time is a measure of the extrinsic pathway of coagulation that is used to determine the clotting tendency of blood. The International Normalized Ratio is the ratio of a patient's prothrombin time to a normal (control) sample.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Mean Change From Baseline to Maximum Value in Phase II of the Study for International Normalized Ratio (Prothrombin Time) [units: ratio] Mean (Standard Deviation)	0.030 (0.0663)	0.042 (0.1094)

16. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase II of the Study for Partial Thromboplastin Time and Prothrombin Time
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline. Partial thromboplastin time is a performance indicator detecting abnormalities in blood clotting.
Time Frame	Baseline to study completion (up to 878 days for Phase II)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Mean Change From Baseline to Maximum Value in Phase II of the Study for Partial Thromboplastin Time and Prothrombin Time [units: seconds (sec)]		

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Mean (Standard Deviation)		
Partial thromboplastin time	2.10 (1.985)	2.62 (3.175)
Prothrombin time	0.0 (0.57)	0.2 (1.19)

17. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Albumin
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg /Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg /Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg / Lapatinib 1500 mg	Phase I: Pazopanib 800 mg / Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Albumin [units: grams per liter (g/L)] Mean (Standard Deviation)	-4.25 (4.573)	-6.17 (5.707)	-3.80 (1.924)	-5.17 (3.545)	-13.66 (16.959)	-7.17 (4.215)

18. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Alkaline Phosphatase, Alanine Aminotransferase, Aspartate Aminotransferase, and Lactate Dehydrogenase
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID

	Description
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Alkaline Phosphatase, Alanine Aminotransferase, Aspartate Aminotransferase, and Lactate Dehydrogenase [units: International Units per Liter (IU/L)] Mean (Standard Deviation)						
Alkaline phosphatase	9.8 (11.47)	22.8 (39.55)	31.2 (53.60)	15.8 (22.66)	22.0 (28.54)	22.0 (47.15)
Alanine aminotransferase	36.8 (66.35)	139.5 (204.81)	47.0 (48.09)	33.2 (25.25)	4.8 (7.19)	47.7 (56.43)
Aspartate aminotransferase	15.0 (31.72)	49.3 (71.63)	13.8 (15.71)	8.8 (7.03)	13.5 (16.20)	19.3 (18.47)
Lactate dehydrogenase	148.0 (96.42)	127.0 (144.60)	46.0 (35.86)	321.2 (534.42)	124.7 (136.46)	116.8 (59.26)

19. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Amylase and Lipase
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Amylase and Lipase [units: Units per liter (U/L)] Mean (Standard Deviation)						
Amylase	24.3 (36.42)	24.4 (17.04)	27.3 (66.4)	31.0 (38.96)	44.4 (52.52)	23.3 (39.38)
Lipase	147.0 (292.02)	23.3 (44.98)	33.0 (56.79)	151.8 (230.63)	67.3 (101.83)	7.8 (21.09)

20. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Total Bilirubin and Creatinine
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)

Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Total Bilirubin and Creatinine [units: micromoles per liter (µmol/l)] Mean (Standard Deviation)						
Total bilirubin	-0.000 (4.6307)	2.613 (2.5162)	3.368 (2.1520)	6.130 (6.0799)	4.135 (3.8089)	6.398 (3.8952)
Creatinine	4.420 (15.3113)	8.367 (11.3656)	7.336 (6.6049)	6.893 (6.6297)	9.727 (9.7448)	12.005 (19.3179)

21. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Calcium, Glucose, Potassium, Magnesium, Inorganic Phosphorus, Sodium, and Urea
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Calcium, Glucose, Potassium, Magnesium, Inorganic Phosphorus, Sodium, and Urea [units: millimoles per liter (mmol/l)]						

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Mean (Standard Deviation)						
Calcium	-0.062 (0.0250)	-0.045 (0.1173)	0.036 (0.0572)	0.061 (0.0874)	0.047 (0.1155)	-0.014 (0.1166)
Glucose	0.56 (1.385)	3.35 (6.653)	1.20 (1.114)	1.02 (2.654)	1.55 (0.589)	0.65 (0.934)
Potassium	0.075 (0.4992)	0.400 (0.3033)	0.420 (0.3033)	0.500 (0.2608)	0.600 (0.5967)	0.183 (0.2229)
Magnesium	0.069 (0.0237)	-0.019 (0.0573)	0.058 (0.0463)	0.051 (0.0510)	0.043 (0.0615)	0.056 (0.0920)
Sodium	-1.000 (1.8257)	0.500 (2.0736)	1.800 (1.6432)	1.333 (2.0656)	1.500 (4.5497)	0.000 (0.6325)
Urea	1.9 (0.18)	0.6 (1.18)	0.8 (1.74)	1.1 (1.27)	0.9 (1.20)	1.7 (1.72)
Inorganic phosphorus	0.02 (0.168)	0.11 (0.186)	0.41 (0.553)	0.16 (0.164)	0.01 (0.129)	0.25 (0.185)

22. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Thyroxine
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD

	Description
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Thyroxine [units: picomoles per liter (pmol/l)] Mean (Standard Deviation)	-0.740 (2.8496)	-1.498 (1.8681)	1.105 (3.6173)	1.879 (2.8191)	0.377 (3.9731)	-0.781 (1.0040)

23. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Free T3 (Triiodothyronine)
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline. For some arms, data were not collected for either baseline or post-baseline assessments.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg /Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg /Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg / Lapatinib 1500 mg	Phase I: Pazopanib 800 mg / Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	0	0	5	0	6	0
Mean Change From Baseline to Maximum Value in Phase I of the Study for Free T3 (Triiodothyronine) [units: picomoles per liter (pmol/l)] Mean (Standard Deviation)			-0.07 (0.222)		-0.94 (1.291)	

24. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Thyroid Stimulating Hormone
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Thyroid Stimulating Hormone [units: milliunits per liter (mU/L)] Mean (Standard Deviation)	-0.5068 (1.99588)	0.1900 (0.38931)	0.6543 (0.73309)	0.6660 (0.70497)	0.6080 (11.10117)	2.2940 (1.25335)

25. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Total T3
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided chemistry measurements at both baseline and post-baseline. For some arms, data were not collected for either baseline or post-baseline assessments.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	0	7	0	0
Mean Change From Baseline to Maximum Value in Phase I of the Study for Total T3 [units: nanomoles per liter (nmol/l)] Mean (Standard Deviation)	-0.071 (0.1113)	0.214 (0.2851)		0.004 (0.0028)		

26. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Hemoglobin
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)

Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	6	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Hemoglobin [units: grams per Liter (g/L)] Mean (Standard Deviation)	-7.25 (14.975)	-7.83 (12.999)	-4.80 (9.834)	-3.33 (13.095)	-16.17 (9.867)	-21.02 (59.642)

27. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Hematocrit

Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline. The hematocrit is the proportion of blood volume that is occupied by red blood cells.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	6	6	6
Mean Change From Baseline to Maximum Value in Phase I of the Study for Hematocrit [units: percent] Mean (Standard Deviation)	-0.02 (0.034)	-0.02 (0.029)	-0.02 (0.023)	0.00 (0.027)	-0.09 (0.103)	0.01 (0.024)

28. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in the Study for Lymphocytes, Neutrophils, Platelet Count, and White Blood Count
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	6	6	6
Mean Change From Baseline to Maximum Value in the Study for Lymphocytes, Neutrophils, Platelet Count, and White Blood Count [units: giga (10^9) per liter (GI/L)]						

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Mean (Standard Deviation)						
Lymphocytes, n=3, 6, 4, 6, 6, 6	-0.377 (0.4611)	-0.120 (0.4291)	-0.153 (0.3083)	-0.032 (0.2807)	-0.218 (0.2316)	-0.250 (0.3017)
Total Neutrophils, n=3, 6, 4, 6, 6, 6	-0.693 (1.0775)	-3.000 (3.2727)	-1.370 (1.5036)	-0.595 (0.8783)	-1.723 (1.7320)	-0.617 (2.7154)
Platelet count, n=4, 6, 5, 6, 6, 6	-12.3 (30.08)	-74.7 (74.18)	-65.4 (32.65)	-25.3 (40.00)	-35.5 (54.72)	-61.8 (32.17)
White blood cell count, n=4, 6, 5, 6, 6, 6	-0.845 (1.0849)	-2.933 (3.6335)	-1.950 (2.1249)	-0.850 (0.9072)	-1.717 (2.2355)	-0.850 (2.4468)

29. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for International Normalized Ratio (Prothrombin Time)
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline. Prothrombin time is a measure of the extrinsic pathway of coagulation that is used to determine the clotting tendency of blood. The International Normalized Ratio is the ratio of a patient's prothrombin time to a normal (control) sample.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phases I and II. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID

	Description
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	6	6	5
Mean Change From Baseline to Maximum Value in Phase I of the Study for International Normalized Ratio (Prothrombin Time) [units: ratio] Mean (Standard Deviation)	0.077 (0.0866)	-0.023 (0.0638)	0.056 (0.0472)	0.000 (0.1097)	0.015 (0.0764)	0.006 (0.0134)

30. Primary Outcome Measure:

Measure Title	Mean Change From Baseline to Maximum Value in Phase I of the Study for Partial Thromboplastin Time and Prothrombin Time
Measure Description	Change from baseline is calculated as the maximum changed value in the study minus the value at Baseline. Partial thromboplastin time is a performance indicator detecting abnormalities in blood clotting.
Time Frame	Baseline to study completion (up to 844 days for Phase I)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I. Data are presented for only those participants who provided hematology measurements at both baseline and post-baseline.

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	6	6	5
Mean Change From Baseline to Maximum Value in Phase I of the Study for Partial Thromboplastin Time and Prothrombin Time [units: seconds (sec)] Mean (Standard Deviation)						
Partial thromboplastin time	1.10 (1.299)	2.88 (1.986)	2.62 (5.545)	-0.38 (6.122)	2.18 (2.082)	1.00 (1.093)
Prothrombin time	0.38 (0.532)	0.47 (0.940)	0.64 (0.981)	-0.02 (0.796)	1.07 (1.722)	0.56 (0.885)

31. Primary Outcome Measure:

Measure Title	Number of Participants Experiencing a Dose-limiting Toxicity at the Indicated Dose

Measure Description	A dose-limiting toxicity (DLT) is defined as predefined adverse events or events that prevented participants from receiving 75% of their scheduled doses or from starting their next treatment period. The dose at which no more than 1 out of 6 participants experiences a DLT is defined as the optimally tolerated regimen. The OTR is important because it determines the highest dose combination that can be given without significant toxicity.
Time Frame	Cycle 1 in Phase I (up to Day 28)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase I

Reporting Groups

	Description
Phase I: Pazopanib 200 mg/Lapatinib 1500 mg	Pazopanib 200 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 1500 mg	Pazopanib 800 mg OD and Lapatinib 1500 mg OD
Phase I: Pazopanib 800 mg/Lapatinib 500 mg	Pazopanib 800 mg OD and Lapatinib 500 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 750 mg	Pazopanib 800 mg OD and Lapatinib 750 mg BID
Phase I: Pazopanib 800 mg/Lapatinib 1000 mg	Pazopanib 800 mg OD and Lapatinib 1000 mg BID
Phase I: Pazopanib 600 mg/Lapatinib 1000 mg	Pazopanib 600 mg BID and Lapatinib 1000 mg BID

Measured Values

	Phase I: Pazopanib 200 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 500 mg	Phase I: Pazopanib 800 mg/ Lapatinib 750 mg	Phase I: Pazopanib 800 mg/ Lapatinib 1000 mg	Phase I: Pazopanib 600 mg/ Lapatinib 1000 mg
Number of Participants Analyzed	4	6	5	7	6	6
Number of Participants Experiencing a Dose-limiting Toxicity at the Indicated Dose [units: participants]	0	1	1	1	1	1

32. Primary Outcome Measure:

Measure Title	Overall Response (OR) in Phase II Based GlaxoSmithKline's Evaluation
Measure Description	OR is the number of participants whose response was classified as a complete response or partial response (disappearance of enhancing tumor (ET) or reduction of ET by >=50%, respectively, on consecutive scans [CS] >=1 month (m) apart, off steroids, and neurologically stable/improved), progressive disease (increase of ET of >=25% on CS >=1 m apart or neurologically worse, and steroids stable/increased), or stable disease (all other situations) per MacDonald criteria. Participants were evaluated with magnetic resonance imaging. Baseline and the 4- and 8-w assessments are categorized as <8 w.
Time Frame	Date of first dose of study drug to date of documented and confirmed progression, or to date of death due to any cause (assessed at baseline, 4 and 8 weeks, and every 8 weeks thereafter until study withdrawal; up to Day 878)
Safety Issue?	No

Analysis Population Description

All-treated Population in Phase II who also had a response assessment

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed EGFRvIII and/or PTEN.
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Overall Response (OR) in Phase II Based GlaxoSmithKline's Evaluation [units: participants]		
Complete response	0	0
Partial response	1	2
Stable disease, >=8 weeks	7	6
Progressive disease, <8 weeks	7	8
Progressive disease	4	6

33. Primary Outcome Measure:

Measure Title	Overall Response (OR) in Phase II Based on the Investigator-assigned Response
Measure Description	OR is the number of participants whose response was classified as a complete response or partial response (disappearance of enhancing tumor (ET) or reduction of ET by >=50%, respectively, on consecutive scans [CS] >=1 month (m) apart, off steroids, and neurologically stable/improved), progressive disease (increase of ET of >=25% on CS >=1 m apart or neurologically worse, and steroids stable/increased), or stable disease (all other situations) per MacDonald criteria. Participants were evaluated with magnetic resonance imaging. Baseline and the 4- and 8-w assessments are categorized as <8 w.
Time Frame	Date of first dose of study drug to date of documented and confirmed progression, or to date of death due to any cause (assessed at baseline, 4 and 8 weeks, and every 8 weeks thereafter until study withdrawal; up to Day 878)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II who also had a response assessment.

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Overall Response (OR) in Phase II Based on the Investigator-assigned Response [units: participants]		
Complete response	0	0
Partial response	1	1
Stable disease, >=8 weeks	7	7
Progressive disease, <8 weeks	7	9
Progressive disease	4	5

34. Primary Outcome Measure:

Measure Title	Overall Response (OR) in Phase II Based on an Independent Radiologist's Review
Measure Description	OR is the number of participants whose response was classified as a complete response or partial response (disappearance of enhancing tumor (ET) or reduction of ET by >=50%, respectively, on consecutive scans [CS] >=1 month (m) apart, off steroids, and neurologically stable/improved), progressive disease (increase of ET of >=25% on CS >=1 m apart or neurologically worse, and steroids stable/increased), or stable disease (all other situations) per MacDonald criteria. Participants were evaluated with magnetic resonance imaging. Baseline and the 4- and 8-w assessments are categorized as <8 w.
Time Frame	Date of first dose of study drug to date of documented and confirmed progression, or to date of death due to any cause (assessed at baseline, 4 and 8 weeks, and every 8 weeks thereafter until study withdrawal; up to Day 878)
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II who also had a response assessment

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed EGFRvIII and/or PTEN.
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Overall Response (OR) in Phase II Based on an Independent Radiologist's Review [units: participants]		
Complete response	0	0
Partial response	0	0
Stable disease, >=8 weeks	5	4
Progressive disease, <8 weeks	5	8
Progressive disease	4	6

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Unconfirmed partial response	4	4

35. Primary Outcome Measure:

Measure Title	Progression-free Survival at 6 Months
Measure Description	Progression-free survival (PFS) analysis was performed on all participants. PFS is presented as the number of participants experiencing disease progression or death due to any cause. Participants who are alive and have not progressed at the time of analysis are considered censored, and the date associated with the last visit with disease assessment will be used. The participants who are still alive and whose follow-up extends to at least 6 months are considered At Risk.
Time Frame	Date of the first dose of study drug to 6 months
Safety Issue?	No

Analysis Population Description

All-treated Population for Phase II

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Progression-free Survival at 6 Months [units: participants]		
Disease progression at or prior to 6 months	15	16
Death at or prior to 6 months	0	2
Censored at or prior to 6 months	4	1
At risk beyond 6 months	0	3

36. Secondary Outcome Measure:

Measure Title	Phase I: Pharmacokinetic Parameters Including AUC(0-24), [AUC(0-12) for Patients on Twice Daily Administration], Cmax, the Time to Maximum Observed Concentration (Tmax) and C24 of Pazopanib and Lapatinib When Administered in Combination With EIAC.
Measure Description	
Time Frame	Completed during first cycle of treatment.
Safety Issue?	No

Outcome Measure Data Not Reported

37. Secondary Outcome Measure:

Measure Title	Phase II: Pharmacokinetic Parameters Including AUC(0-24), [AUC(0-12) for Patients on Twice Daily Administration], Cmax, Tmax, and C24 of Pazopanib and Lapatinib, as Appropriate, When Administered Together in Combination With Non-EIAC.
Measure Description	
Time Frame	Completed during first cycle of treatment.
Safety Issue?	No

Outcome Measure Data Not Reported

38. Secondary Outcome Measure:

Measure Title	Phase II: Plasma Concentrations of the Circulating Biomarkers VEGF, sVEGFR-1, and sVEGFR-2.
Measure Description	
Time Frame	Completed during first cycle of treatment.
Safety Issue?	No

Outcome Measure Data Not Reported

39. Secondary Outcome Measure:

Measure Title	Progression-free Survival
Measure Description	Progression-free survival (PFS) analysis was performed on all participants. PFS is presented as the number of participants experiencing disease progression or death due to any cause. Participants who are alive and have not progressed at the time of analysis are considered censored, and the date associated with the last visit with disease assessment will be used.

Time Frame	Date of the first dose of study drug to the date of documented and confirmed progression by Mac Donald criteria, or to date of death due to any cause (up to Day 878)
Safety Issue?	No

Analysis Population Description
All-treated Population for Phase II

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Progression-free Survival [units: participants]		
Disease progression	15	18
Death	0	2
Censored	4	2

40. Secondary Outcome Measure:

Measure Title	Time to Disease Progression or Death Due to Any Cause
Measure Description	
Time Frame	Date of the first dose of study drug to the date of documented and confirmed progression by Mac Donald criteria, or to date of death due to any cause (up to Day 878)
Safety Issue?	No

Analysis Population Description
All-treated Population for Phase II

Reporting Groups

	Description
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (BID) and lapatinib 1000 mg OD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg OD and lapatinib 1000 mg OD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Measured Values

	Phase II: Biomarker Positive	Phase II: Biomarker Negative
Number of Participants Analyzed	19	22
Time to Disease Progression or Death Due to Any Cause [units: days] Median (95% Confidence Interval)	62 (56 to 90)	56 (45 to 113)

Reported Adverse Events

Time Frame	Serious adverse events (SAEs) and non-serious AES in Phases I and II were collected from Day 1 of study treatment to study completion (up to 844 days for Phase I; up to 878 days for Phase II).
Additional Description	[Not specified]

Reporting Groups

	Description
Phase I: Pazopanib 200-800 mg/ Lapatinib 500-1500 mg	Starting dose of oral pazopanib of 200 milligrams (mg) once daily (OD) and oral lapatinib 1500 mg OD. The dose of pazopanib (200-800 mg) and lapatinib (500-1500 mg) in cohorts enrolled subsequent to the first dose cohort was determined by the toxicity profile of the combination therapy and the pharmacokinetic results from the prior cohort.
Phase II: Biomarker Positive	All participants received pazopanib 400 mg twice daily (QD) and lapatinib 1000 mg QD. Biomarker-positive participants were those who expressed epithelial growth factor receptor vIII (EGFRvIII) and/or phosphate and tensin homolog (PTEN).
Phase II: Biomarker Negative	All participants received pazopanib 400 mg QD and lapatinib 1000 mg QD. Biomarker-negative participants were those who did not express either EGFRvIII and/or PTEN.

Serious Adverse Events

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	15/34 (44.12%)	6/19 (31.58%)	8/22 (36.36%)
Blood and lymphatic system disorders			
Thrombocytopenia [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Endocrine disorders			
Hypothyroidism [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Gastrointestinal disorders			
Abdominal pain [A] †	0/34 (0%)	0/19 (0%)	1/22 (4.55%)
Diarrhea [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Nausea [A] †	2/34 (5.88%)	0/19 (0%)	0/22 (0%)
Pancreatitis [A] †	0/34 (0%)	2/19 (10.53%)	0/22 (0%)
Vomiting [A] †	3/34 (8.82%)	0/19 (0%)	0/22 (0%)
General disorders			
Asthenia [A] †	0/34 (0%)	0/19 (0%)	1/22 (4.55%)
Fatigue [A] †	2/34 (5.88%)	0/19 (0%)	1/22 (4.55%)
Pyrexia [A] †	2/34 (5.88%)	0/19 (0%)	0/22 (0%)
Infections and infestations			
Infection [A] †	0/34 (0%)	0/19 (0%)	1/22 (4.55%)
Lobar pneumonia [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Pneumonia [A] †	0/34 (0%)	0/19 (0%)	1/22 (4.55%)
Pneumonia streptococcal [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Injury, poisoning and procedural complications			
Brain herniation [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Femoral neck fracture [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Pubis fracture [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Investigations			
Alanine aminotransferase increased [A] †	1/34 (2.94%)	0/19 (0%)	1/22 (4.55%)
Aspartate aminotransferase increased [A] †	1/34 (2.94%)	0/19 (0%)	1/22 (4.55%)
Transaminases increased [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Metabolism and nutrition disorders			
Hyperglycemia [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Musculoskeletal and connective tissue disorders			
Muscular weakness [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor hemorrhage [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Nervous system disorders			
Cerebral hemorrhage [A] †	0/34 (0%)	0/19 (0%)	1/22 (4.55%)
Convulsion [A] †	1/34 (2.94%)	1/19 (5.26%)	4/22 (18.18%)
Headache [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Hemiparesis [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Partial seizures [A] †	0/34 (0%)	0/19 (0%)	1/22 (4.55%)
Speech disorder [A] †	0/34 (0%)	1/19 (5.26%)	0/22 (0%)
Syncope [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Psychiatric disorders			
Confusional state [A] †	2/34 (5.88%)	1/19 (5.26%)	0/22 (0%)

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Mental status changes [A] †	0/34 (0%)	1/19 (5.26%)	0/22 (0%)
Mood altered [A] †	0/34 (0%)	1/19 (5.26%)	0/22 (0%)
Respiratory, thoracic and mediastinal disorders			
Aspiration [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Dyspnea [A] †	1/34 (2.94%)	0/19 (0%)	0/22 (0%)
Pneumonitis [A] †	0/34 (0%)	1/19 (5.26%)	0/22 (0%)
Pulmonary embolism [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Vascular disorders			
Deep vein thrombosis [A] †	0/34 (0%)	0/19 (0%)	1/22 (4.55%)

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

Other Adverse Events

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

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	33/34 (97.06%)	18/19 (94.74%)	22/22 (100%)
Blood and lymphatic system disorders			
Anemia [A] †	3/34 (8.82%)	1/19 (5.26%)	4/22 (18.18%)
Leukopenia [A] †	1/34 (2.94%)	1/19 (5.26%)	3/22 (13.64%)
Lymphopenia [A] †	3/34 (8.82%)	5/19 (26.32%)	6/22 (27.27%)
Neutropenia [A] †	4/34 (11.76%)	0/19 (0%)	1/22 (4.55%)
Thrombocytopenia [A] †	4/34 (11.76%)	1/19 (5.26%)	2/22 (9.09%)
Cardiac disorders			

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Sinus bradycardia [A] †	0/34 (0%)	0/19 (0%)	2/22 (9.09%)
Ear and labyrinth disorders			
Deafness unilateral [A] †	2/34 (5.88%)	0/19 (0%)	1/22 (4.55%)
Tinnitus [A] †	2/34 (5.88%)	0/19 (0%)	1/22 (4.55%)
Endocrine disorders			
Cushingoid [A] †	0/34 (0%)	2/19 (10.53%)	2/22 (9.09%)
Eye disorders			
Vision blurred [A] †	9/34 (26.47%)	1/19 (5.26%)	5/22 (22.73%)
Gastrointestinal disorders			
Abdominal pain [A] †	1/34 (2.94%)	1/19 (5.26%)	2/22 (9.09%)
Constipation [A] †	4/34 (11.76%)	1/19 (5.26%)	4/22 (18.18%)
Diarrhea [A] †	19/34 (55.88%)	12/19 (63.16%)	14/22 (63.64%)
Flatulence [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Hemorrhoidal hemorrhage [A] †	2/34 (5.88%)	0/19 (0%)	0/22 (0%)
Nausea [A] †	9/34 (26.47%)	5/19 (26.32%)	3/22 (13.64%)
Oral pain [A] †	0/34 (0%)	0/19 (0%)	2/22 (9.09%)
Vomiting [A] †	2/34 (5.88%)	2/19 (10.53%)	3/22 (13.64%)
General disorders			
Asthenia [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Edema peripheral [A] †	3/34 (8.82%)	1/19 (5.26%)	2/22 (9.09%)
Fatigue [A] †	16/34 (47.06%)	11/19 (57.89%)	10/22 (45.45%)
Gait disturbance [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Mucosal inflammation [A] †	3/34 (8.82%)	1/19 (5.26%)	1/22 (4.55%)
Pyrexia [A] †	0/34 (0%)	0/19 (0%)	2/22 (9.09%)
Hepatobiliary disorders			
Hyperbilirubinaemia/blood bilirubin increased [A] †	1/34 (2.94%)	1/19 (5.26%)	5/22 (22.73%)
Infections and infestations			
Candidiasis [A] †	1/34 (2.94%)	1/19 (5.26%)	1/22 (4.55%)
Urinary tract infection [A] †	2/34 (5.88%)	0/19 (0%)	1/22 (4.55%)
Injury, poisoning and procedural complications			
Contusion [A] †	1/34 (2.94%)	0/19 (0%)	3/22 (13.64%)
Investigations			
Alanine aminotransferase increased [A] †	8/34 (23.53%)	2/19 (10.53%)	2/22 (9.09%)
Aspartate aminotransferase increased [A] †	4/34 (11.76%)	2/19 (10.53%)	1/22 (4.55%)
Blood alkaline phosphatase increased [A] †	2/34 (5.88%)	1/19 (5.26%)	0/22 (0%)
Blood amylase increased [A] †	1/34 (2.94%)	3/19 (15.79%)	2/22 (9.09%)
Blood lactate dehydrogenase increased [A] †	1/34 (2.94%)	1/19 (5.26%)	3/22 (13.64%)
Blood urea increased [A] †	1/34 (2.94%)	0/19 (0%)	3/22 (13.64%)
Lipase increased [A] †	3/34 (8.82%)	2/19 (10.53%)	3/22 (13.64%)
Neutrophil count decreased [A] †	0/34 (0%)	2/19 (10.53%)	2/22 (9.09%)
Weight decreased [A] †	1/34 (2.94%)	2/19 (10.53%)	1/22 (4.55%)
Weight increased [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
White blood cell count decreased [A] †	2/34 (5.88%)	0/19 (0%)	0/22 (0%)
Metabolism and nutrition disorders			

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Decreased appetitie [A] †	3/34 (8.82%)	2/19 (10.53%)	1/22 (4.55%)
Dehydration [A] †	0/34 (0%)	0/19 (0%)	3/22 (13.64%)
Hyperglycemia [A] †	2/34 (5.88%)	3/19 (15.79%)	6/22 (27.27%)
Hyperkalaemia [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Hypoalbuminaemia [A] †	0/34 (0%)	1/19 (5.26%)	2/22 (9.09%)
Hypocalcaemia [A] †	1/34 (2.94%)	1/19 (5.26%)	2/22 (9.09%)
Hypoglycaemia [A] †	0/34 (0%)	0/19 (0%)	2/22 (9.09%)
Hypokalaemia [A] †	0/34 (0%)	1/19 (5.26%)	2/22 (9.09%)
Hypomagnesemia [A] †	1/34 (2.94%)	0/19 (0%)	4/22 (18.18%)
Hypophosphataemia [A] †	0/34 (0%)	0/19 (0%)	3/22 (13.64%)
Musculoskeletal and connective tissue disorders			
Arthralgia [A] †	3/34 (8.82%)	1/19 (5.26%)	1/22 (4.55%)
Back pain [A] †	2/34 (5.88%)	2/19 (10.53%)	0/22 (0%)
Joint stiffness [A] †	2/34 (5.88%)	0/19 (0%)	0/22 (0%)
Muscle spasms [A] †	0/34 (0%)	0/19 (0%)	2/22 (9.09%)
Muscular weakness [A] †	5/34 (14.71%)	0/19 (0%)	2/22 (9.09%)
Musculoskeletal pain [A] †	0/34 (0%)	0/19 (0%)	3/22 (13.64%)
Myalgia [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Pain in extremity [A] †	1/34 (2.94%)	1/19 (5.26%)	1/22 (4.55%)
Nervous system disorders			
Amnesia [A] †	4/34 (11.76%)	5/19 (26.32%)	1/22 (4.55%)
Aphasia [A] †	4/34 (11.76%)	0/19 (0%)	0/22 (0%)

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Ataxia [A] †	1/34 (2.94%)	2/19 (10.53%)	4/22 (18.18%)
Balance disorder [A] †	2/34 (5.88%)	0/19 (0%)	0/22 (0%)
Cognitive disorder [A] †	2/34 (5.88%)	3/19 (15.79%)	4/22 (18.18%)
Convulsion [A] †	4/34 (11.76%)	2/19 (10.53%)	4/22 (18.18%)
Cranial nerve disorder [A] †	1/34 (2.94%)	0/19 (0%)	3/22 (13.64%)
Dizziness [A] †	0/34 (0%)	3/19 (15.79%)	1/22 (4.55%)
Dysgeusia [A] †	0/34 (0%)	2/19 (10.53%)	1/22 (4.55%)
Headache [A] †	9/34 (26.47%)	7/19 (36.84%)	8/22 (36.36%)
Hemiparesis [A] †	3/34 (8.82%)	1/19 (5.26%)	1/22 (4.55%)
Memory impairment [A] †	1/34 (2.94%)	0/19 (0%)	2/22 (9.09%)
Partial seizures [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Peripheral motor neuropathy [A] †	2/34 (5.88%)	3/19 (15.79%)	3/22 (13.64%)
Peripheral sensory neuropathy [A] †	4/34 (11.76%)	3/19 (15.79%)	5/22 (22.73%)
Pyramidal tract syndrome [A] †	2/34 (5.88%)	2/19 (10.53%)	1/22 (4.55%)
Somnolence [A] †	2/34 (5.88%)	2/19 (10.53%)	3/22 (13.64%)
Speech disorder [A] †	1/34 (2.94%)	1/19 (5.26%)	3/22 (13.64%)
Tremor [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Psychiatric disorders			
Confusional state [A] †	0/34 (0%)	4/19 (21.05%)	4/22 (18.18%)
Depressed mood [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Insomnia [A] †	4/34 (11.76%)	3/19 (15.79%)	3/22 (13.64%)

	Phase I: Pazopanib 200-800 mg/Lapatinib 500-1500 mg	Phase II: Biomarker Positive	Phase II: Biomarker Negative
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Mood altered/mood swings [A] †	1/34 (2.94%)	2/19 (10.53%)	1/22 (4.55%)
Renal and urinary disorders			
Pollakiuria [A] †	2/34 (5.88%)	0/19 (0%)	0/22 (0%)
Urinary incontinence [A] †	1/34 (2.94%)	0/19 (0%)	2/22 (9.09%)
Reproductive system and breast disorders			
Sexual dysfunction [A] †	0/34 (0%)	2/19 (10.53%)	2/22 (9.09%)
Respiratory, thoracic and mediastinal disorders			
Cough [A] †	3/34 (8.82%)	0/19 (0%)	4/22 (18.18%)
Dyspnea [A] †	2/34 (5.88%)	0/19 (0%)	1/22 (4.55%)
Epistaxis [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Oropharyngeal pain [A] †	2/34 (5.88%)	0/19 (0%)	1/22 (4.55%)
Skin and subcutaneous tissue disorders			
Alopecia [A] †	1/34 (2.94%)	0/19 (0%)	2/22 (9.09%)
Dermatitis acneiform [A] †	3/34 (8.82%)	1/19 (5.26%)	5/22 (22.73%)
Exfoliative rash [A] †	1/34 (2.94%)	0/19 (0%)	2/22 (9.09%)
Hair color changes [A] †	0/34 (0%)	1/19 (5.26%)	1/22 (4.55%)
Rash [A] †	5/34 (14.71%)	8/19 (42.11%)	4/22 (18.18%)
Vascular disorders			
Deep vein thrombosis [A] †	3/34 (8.82%)	0/19 (0%)	0/22 (0%)
Hypertension [A] †	9/34 (26.47%)	3/19 (15.79%)	9/22 (40.91%)

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

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.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

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