ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 06/07/2012

ClinicalTrials.gov ID: NCT00367679

Study Identification

Unique Protocol ID:	VEG105290
Brief Title:	Pazopanib As Pre-Surgical Therapy In Treatment-Naive Subjects With Non-Small Cell Lung Cancer
Official Title:	A Phase II Open-Label Multicenter Study to Evaluate the Safety and Efficacy of Pazopanib (GW786034) as Neoadjuvant Therapy in Treatment-Naïve Subjects With Stage IA, IB, IIA or IIB (to T2) Resectable Non-Small Cell Lung Cancer (NSCLC)
Secondary IDs:	

Study Status

Record Verification:	May 2012
Overall Status:	Completed
Study Start:	November 2006
Primary Completion:	April 2008 [Actual]
Study Completion:	April 2008 [Actual]

Sponsor/Collaborators

Sponsor:	GlaxoSmithKline
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	
IND/IDE Protocol?:	Yes

IND/IDE Information:	Grantor: CDER IND/IDE Number: 65,747 Serial Number: 0099 Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration

Study Description

Brief Summary:	This is a phase 2 open-label, multicenter, non-randomized study to evaluate the safety and efficacy of oral pazopanib as neoadjuvant treatment for patients with stage 1A, 1B, IIA or IIB (to T2) resectable Non-Small Cell Lung Cancer (NSCLC).
Detailed Description:	

Conditions

Conditions:	Non-Small Cell Lung Cancer Lung Cancer, Non-Small Cell
Keywords:	pazopanib I-ELCAP non-small cell lung cancer antiangiogenesis NSCLC GW786034

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:	Safety/Efficacy Study
Enrollment:	35 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Single Arm 800 mg pazopanib oral daily	Drug: Pazopanib Pazopanib is an oral, potent, multi-target receptor tyrosine kinase inhibitor of VEGFR-1, -2, -3, PDGFR-alpha and -beta and c-kit. Subjects were to receive 800 mg oral pazopanib daily for a minimum of 2 weeks to a maximum of 6 weeks. Other Names: • Pazopanib

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	21 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion criteria:

- Signed, written informed consent provided prior to performing any study-specific procedures or assessments. Subject must be willing to comply with treatment and follow-up.
- Subjects ≥21 years of age with a life expectancy of ≥12 weeks
- The time between initial diagnosis and the scheduled surgery date allows for the subject to receive a minimum of 2 weeks or a maximum of 6 weeks treatment with pazopanib. Note: At least 4 weeks must be available between the diagnostic biopsy and surgery to allow for 1) one-week delay following the diagnostic biopsy prior to first dose of study drug, 2) minimum of 2 weeks on study drug, and 3) minimum of 1 week wash out prior to surgery.
- Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0 or 1.

- Histologically- or cytologically-confirmed Stage IA, IB, IIA, or IIB (to T2) NSCLC according to the International Staging System [Mountain, 1997] and must be scheduled for surgical resection.
- Disease must consist of only a single lesion and must be measurable according to high-resolution CT scan-assisted volumetric measurement [Yankelevitz, 2000, Armato, 2004]. In addition to the measurable single lesion, other small indeterminate nodules may also be present
- No approved or investigational anti-cancer therapy concurrently or in the 6 months prior to start of study drug, including surgery, tumor embolization, chemotherapy, radiation therapy, immunotherapy, hormone therapy, biologic therapy, or anti-angiogegneic therapy (e.g., inhibitors of VEGF or VEGFR).
- Fresh tumor biopsy for apoptosis and relevant biomarker analyses must be obtained within 30 to 8 days of first dose of study drug and must be available for all subjects prior to start of pazopanib treatment.
- System (Laboratory Values)
- Hematologic:Absolute neutrophil count (ANC)(≥ 1.5 X 109/L), Hemoglobin (≥9 g/dL), Platelets(≥100 X 109/L)
- Hepatic:Albumin (≥ 2.5 g/dL), Serum bilirubin(≤1.5 X upper limit of normal (ULN) unless due to Gilbert's syndrome), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) (≤2.0 X ULN) Renal:Serum creatinine(≤1.5 mg/dL) OR Calculated creatinine clearance (≥30 mL/min), Urine Protein (Trace or +1 by dipstick urinalysis or <1.0 gram determined by 24-hour urine protein analysis.)
- Ability to swallow and retain oral medication
- A female is eligible to enter and participate in this study if she is of:
- Non-childbearing potential (i.e., physiologically incapable of becoming pregnant), including any female who has had:
- A hysterectomy
- A bilateral oophorectomy (ovariectomy)
- A bilateral tubal ligation
- Is post-menopausal:
- Subjects not using hormone replacement therapy (HRT) must have experienced total cessation of menses for ≥1 year and be greater than 45 years in age, OR, in questionable cases, have a follicle stimulating hormone (FSH) value >40mIU/mL and an estradiol value <40pg/mL (<140pmol/L).
- Subjects must discontinue HRT prior to study enrollment due to the potential for inhibition of cytochrome P450 enzymes that metabolize estrogens and progestins. For most forms of HRT, at least 2-4 weeks must elapse between the cessation of HRT and determination of menopausal status; length of this interval depends on the type and dosage of HRT. If a female subject is determined not to be post-menopausal, they must use adequate contraception, as defined immediately below.
- Childbearing potential, including any female who has had a negative serum pregnancy test within 2 weeks prior to the first dose of study treatment, preferably as close to the first dose as possible, and agrees to use adequate contraception. GlaxoSmithKline (GSK)-acceptable contraceptive methods, when used consistently and in accordance with both the product label and the instructions of the physician, are as follow:
- An intrauterine device with a documented failure rate of less than 1% per year
- Vasectomized partner who is sterile prior to the female subject's entry and is the sole sexual partner for that female
- Complete abstinence from sexual intercourse for 14 days before exposure to investigational product, through the dosing period, and for at least 21 days after the last dose of investigational product
- Double-barrier contraception (condom with spermicidal jelly, foam suppository, or film; diaphragm with spermicide; or male condom and diaphragm with spermicide) Note: Oral contraceptives are not reliable due to potential drug-drug interactions.
- Female subjects who are lactating should discontinue nursing prior to the first dose of study drug and should refrain from nursing throughout the treatment period and for 15 days following the last dose of study drug.
- A male 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.
- Subjects must complete all screening assessments as outlined in the protocol

Exclusion criteria:

- Active malignancy or any malignancy in the 6 months prior to first dose of study drug.
- Concurrent disease or condition that would make the subject inappropriate for study participation including (1) any unresolved or unstable, serious toxicity from prior administration of another investigational drug, (2) any serious medical disorder that would interfere with the subject's safety, obtaining informed consent, or compliance with all study related procedures.
- Major surgical procedure, open biopsy, or significant traumatic injury within 4 weeks prior to beginning therapy, or anticipation of the need for a major surgical procedure during the course of the study; minor surgical procedures such as fine needle aspiration or core biopsy within 1 week prior to beginning therapy are also excluded.
- History or clinical evidence of central nervous system (CNS) metastases or leptomeningeal carcinomatosis. Routine screening with CNS imaging studies (computed tomography [CT] or magnetic resonance imaging [MRI]) is required only if clinically indicated.
- History of human immunodeficiency virus (HIV) infection or chronic hepatitis B or C.
- History of hemoptysis
- Malabsorption Syndrome, disease significantly affecting gastrointestinal function, or resection of the stomach or small bowel. Subjects with ulcerative colitis are also excluded
- Active peptic ulcer disease, inflammatory bowel disease, or other gastrointestinal condition increasing the risk of perforation; history of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within 4 weeks prior to beginning therapy
- Active or uncontrolled infection
- Concurrent treatment with an investigational agent or participation in another clinical trial.
- Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to pazopanib
- Has taken/received prohibited medications within specified timeframes.
- Corrected QT interval (QTc) prolongation defined as QTc interval >480 msecs
- History of any one of the following cardiac conditions within the past 6 months: cardia angioplasty or stenting, myocardial infarction,or unstable angina
- History of cerebrovascular accident within the past 6 months
- Has Class II, III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system.
- Poorly controlled hypertension (mean systolic blood pressure (SBP) of ≥140mmHg, or mean diastolic blood pressure (DBP) of ≥ 90mmHg. Note: Initiation or adjustment of anti-hypertensive medication(s) is permitted prior to study entry. The blood pressure (BP) must be re-assessed on two occasions that are separated by a minimum of 5 minutes. The mean SBP/DBP values from both BP assessments must be < 140/90mmHg in order for a subject to be eligible for the study.
- History of untreated deep venous thrombosis (DVT) within the past 6 months (e.g. calf vein thrombosis).
- Presence of any non-healing wound, fracture, or ulcer, or the presence of symptomatic peripheral vascular disease.
- Receiving therapeutic warfarin or heparin as a concurrent medication. Note: prophylactic low-dose warfarin (less than or equal to 2 mg daily) is permitted.
- Evidence of bleeding diathesis or coagulopathy
- Pregnant or lactating female

Contacts/Locations

Study Officials: GSK Clinical Trials
Study Director

GlaxoSmithKline

Locations: Israel
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References

Citations: Altorki N, Guarino M, Lee P, et al. Preoperative treatment with pazopanib (GW786034), a multikinase angiogenesis inhibitor in early-stage non-small cell lung cancer (NSCLC): A proof-of-concept phase II study. JCO, 2008 Vol 26, No 15S (May 20 Supplement), 2008: 7557

Altorki N, Lane ME, Bauer T, Lee PC, Guarino MJ, Pass H, Felip E, Peylan-Ramu N, Gurpide A, Grannis FW, Mitchell JD, Tachdjian S, Swann S, Huff A, Roychowdhury DF, Reeves A, Ottesen LH, Yankelevitz DF. A Phase II Proof-of-Concept Study of Pazopanib (GW786034) Monotherapy in Treatment-Naive Patients With Stage I/II Resectable Non-Small Cell Lung Cancer. [J Clin Oncol]. 2010;10.1200(JCO.2009.23.9749):

Altorki N, Heymach J, Guarino M, et al. A Phase II Study of Pazopanib (GW786034) given Preoperatively in Phase I-II Non-Small Cell Lung Cancer (NSCLC): A Proof of Concept Study. Ann Oncol. 2008;19:viii89 [suppl 8; abstr 2250]).

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Overall Study

	Pazopanib 800 mg
Started	35
Completed	35
Not Completed	0

Baseline Characteristics

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Baseline Measures

	Pazopanib 800 mg
Number of Participants	35
Age, Continuous [units: years] Mean (Standard Deviation)	63.7 (8.84)
Gender, Male/Female [units: participants]	
Female	22
Male	13
Race/Ethnicity, Customized [units: participants]	
White	28
African American/African Heritage	3
Asian	4

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants Achieving Tumor Shrinkage Based on Change in Tumor Volume
Measure Description	Tumor shrinkage was assessed as the change in tumor volume using high-resolution computed tomography scans of the thorax following treatment with pazopanib. Response is defined as the number of participants achieving at least 50% tumor volume reduction following pazopanib treatment. "Responder" is a participant whose tumor volume reduced at least 50% following pazopanib treatment. "Non-responder" is a participant whose tumor volume did not reduce at least 50% following treatment. Tumor assessments were conducted by a central reviewer.
Time Frame	Baseline to at least two weeks or at most six weeks
Safety Issue?	No

Analysis Population Description

Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	35
Number of Participants Achieving Tumor Shrinkage Based on Change in Tumor Volume [units: participants]	
Responder	2
Non-responder	33

Statistical Analysis 1 for Number of Participants Achieving Tumor Shrinkage Based on Change in Tumor Volume

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Percentage of participants with response]
	Estimated Value	5.7
	Confidence Interval	(2-Sided) 95% 0.7 to 19.2
	Estimation Comments	The estimated value given is the percentage of participants who had a response out of the total participants.

2. Secondary Outcome Measure:

Measure Title	Number of Participants Achieving a Clinical Response Based on RECIST

Measure Description	Response is the number of participants achieving either complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumors (RECIST). CR, all detectable tumor has disappeared; PR, a >=30% decrease in the sum of the longest dimensions of the target lesions taking as a reference the baseline sum; Progressive disease (PD), a >=20% increase in target lesions; Stable Disease, small changes not meeting previously given criteria. Confirmation requires at least 2 assessments (conducted by a central reviewer) of CR/PR with at least 4 weeks between the assessments.
Time Frame	Baseline to at least two weeks or at most six weeks
Safety Issue?	No

Analysis Population Description

Safety population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	35
Number of Participants Achieving a Clinical Response Based on RECIST [units: participants]	
Complete response	0
Partial response	3
Stable disease	31
Progressive disease	1

Statistical Analysis 1 for Number of Participants Achieving a Clinical Response Based on RECIST

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Percentage of participants with response]
	Estimated Value	8.6
	Confidence Interval	(2-Sided) 95% 1.8 to 23.1
	Estimation Comments	The estimated value given is the percentage of participants who had a response out of the total participants.

3. Secondary Outcome Measure:

Measure Title	Number of Participants Achieving a >=60% Reduction in Tumor Metabolic Activity Determined as Standard Uptake Value (SUV)
Measure Description	Response is the number of participants whose tumor demonstrated a 60% or greater reduction in metabolic activity (SUV) as measured by positron emission tomography (PET) or PET/computed tomography (PET/CT) at the end of treatment visit relative to baseline. This analysis was not conducted because insufficient data were collected: only three participants had PET/CT data.
Time Frame	Baseline to at least two weeks or at most six weeks
Safety Issue?	No

Analysis Population Description

Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

4. Secondary Outcome Measure:

Measure Title	Number of Participants With Shifts From Baseline to Grade 2 or Greater in Hematology Values

Measure Description	Shifts in hematology values by grade were summarized based on the National Institutes of Health (NIH) Common Terminology Criteria for Adverse Events (Version 3.0 – definitions provided with each parameter below). Shifts to Grade 2 or greater at any point in the study following baseline are reported here.
Time Frame	Baseline to at least three weeks and at most 8 weeks
Safety Issue?	No

Analysis Population Description
Safety Population

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 mg (tablets) administered orally once a day

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	35
Number of Participants With Shifts From Baseline to Grade 2 or Greater in Hematology Values [units: participants]	
Lymphocytes, Grade 2 (<0.8-0.5 x 10^9/L)	5
Lymphocytes, Grade 3 (<0.5-0.2 x 10^9/L)	1
Neutrophils, Grade 2 (<1.5-1.0 x 10^9/L)	4
Neutrophils, Grade 3 (<1.0-0.5 x 10^9/L)	1
White blood cells, Grade 2 (<3.0-2.0 x 10^9/L)	3
White blood cells, Grade 3 (<2.0-1.0 x 10^9/L)	0

5. Secondary Outcome Measure:

Measure Title	Number of Participants With Shifts From Baseline to Grade 2 or Greater in Chemistry Values
Measure Description	Shifts in chemistry values by grade were summarized based on the NIH Common Terminology Criteria for Adverse Events (Version 3.0 – definitions provided with each parameter below). Shifts to Grade 2 or greater at any point in the study following baseline are reported here. ULN = upper limit of normal; Gr = grade; mg = milligrams; dL = deciliter; mmol = millimoles.
Time Frame	Baseline to at least three weeks and at most 8 weeks

Safety Issue?	No

Analysis Population Description
Safety Population

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 mg (tablets) administered orally once a day

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	35
Number of Participants With Shifts From Baseline to Grade 2 or Greater in Chemistry Values [units: participants]	
Alkaline phosphatase, Grade 2 (>2.5-5.0 x ULN)	2
Alanine aminotransferase, Grade 2 (>2.5-5.0 ULN)	6
Alanine aminotransferase, Gr 3 (>5.0-20.0 x ULN)	2
Aspartate aminotransferase, Gr 2 (>2.5-5.0 x ULN)	3
Aspartate aminotransferase, Gr 3 (>5.0-20.0 x ULN)	1
Total bilirubin, Grade 3 (>3.0-10.0 x ULN)	1
Hypocalcemia, Grade 4 (<6.0 mg/dL)	1
Hyperglycemia, Grade 2 (>160-250 mg/dL)	4
Hyperkalemia, Grade 3 (>6.0-7.0 mmol/L)	1

6. Secondary Outcome Measure:

Measure Title	Number of Participants With the Indicated Change From Baseline in Systolic and Diastolic Blood Pressure
Measure Description	Increases in systolic or diastolic blood pressure values at any point in the study following baseline were summarized. mmHg = millimeters of mercury. Baseline blood pressure values as well as the change from baseline experienced are given in the category titles.
Time Frame	Baseline to at least three weeks and at most 8 weeks

Safety Issue?	No

Analysis Population Description
Safety Population

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 mg (tablets) administered orally once a day

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	35
Number of Participants With the Indicated Change From Baseline in Systolic and Diastolic Blood Pressure [units: participants]	
Systolic, BL: 90-139 mmHg; up to 140-169 mmHg	12
Diastolic, BL: 50-89 mmHg; up to 90-109 mmHg	4

7. Secondary Outcome Measure:

Measure Title	Number of Cells Exhibiting Apoptosis in Participant Samples
Measure Description	Tumor cells from pre-treatment and post-operative biopsies were to have been analyzed to determine the number of cells that were exhibiting apoptosis. Due to the limited quantity of tissue in pre- and post-treatment biopsy samples, these assays were not performed.
Time Frame	Baseline to at least three weeks and at most 8 weeks (surgery date)
Safety Issue?	No

Analysis Population Description
Tissue from Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

8. Secondary Outcome Measure:

Measure Title	Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Genes
Measure Description	Gene expression data analysis was performed with GeneSpring GX 7.3.1 (Agilent Technologies). Data were preprocessed using the RMA algorithm. The Benjamini and Hochberg false discovery rate was used for multiple testing corrections. Data below are log-transformed ratios of the post-treatment to pre-treatment expression intensity, indicating the fold increase/decrease in expression of genes. PDGF, platelet-derived growth factor; VEGFR, vascular endothelial growth factor receptor; c-KIT, a protein tyrosine kinase that is a receptor for stem cell factor or “kit” ligand.
Time Frame	Baseline to at least three weeks and at most 8 weeks (surgery date)
Safety Issue?	No

Analysis Population Description

Tumor tissue from Safety Population: all participants who received at least one dose of pazopanib. Only 26 of 35 subjects had sufficient tissue in both pre- and post-treatment samples for analysis.

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 mg (tablets) administered orally once a day

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	26
Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Genes [units: ratio] Median (Standard Deviation)	
Thrombospondin 1	3.234 (1.56)
PDGF-alpha	10.350 (2.433)
PDGF-beta	4.075 (1.504)
VEGF A	-1.129 (0.852)

	Pazopanib 800 mg
VEGF C	3.232 (1.547)
VEGF D	3.569 (2.537)
VEGFR-1	4.258 (1.792)
VEGFR-2	1.943 (1.572)
KIT	1.394 (1.621)
Angiopoietin 1	4.901 (2.066)
Angiopoietin 2	4.207 (1.587)
Transforming growth factor 3	3.054 (1.280)
Fibroblast growth factor 7	3.679 (1.310)

Statistical Analysis 1 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Genes

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0028
	Comments	VEGF D
	Method	t-test, 2 sided
	Comments	Post- versus pretreatment expression levels for each of the indicated genes in response to pazopanib treatment

Statistical Analysis 2 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Genes

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0324
	Comments	VEGF A
	Method	t-test, 2 sided
	Comments	Post- versus pretreatment expression levels for each of the indicated genes in response to pazopanib treatment

Statistical Analysis 3 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Genes

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0082
	Comments	VEGFR-2
	Method	t-test, 2 sided
	Comments	Post- versus pretreatment expression levels for each of the indicated genes in response to pazopanib treatment

Statistical Analysis 4 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Genes

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0082
	Comments	c-KIT
	Method	t-test, 2 sided
	Comments	Post- versus pretreatment expression levels for each of the indicated genes in response to pazopanib treatment

9. Secondary Outcome Measure:

Measure Title	Gene Mutations in Pre- or Post-treatment Tumor Biopsies
Measure Description	Specific genes (KRAS, MYC, TP53, and others) were to have been analyzed for the presence or absence of amplifications or deletions and for the presence, absence, and sequence of point mutations in pre- or post-treatment tumor biopsies. These analyses were not conducted because the potential results were considered to provide overlapping information with those obtained in the transcriptional and proteomic profiling assays that were conducted. The clinical study report indicates that genetic measures were to have been reported separately.
Time Frame	Baseline to at least three weeks and at most 8 weeks (surgery date)
Safety Issue?	No

Analysis Population Description

Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

10. Secondary Outcome Measure:

Measure Title	Intratumoral Levels of Specific Biomarkers
Measure Description	A pre-treatment tumor biopsy from each participant was to have been analyzed by Western blotting to semi-quantitate levels of various proteins related to angiogenesis and/or to the mechanism of action of pazopanib. These assays were not carried out due to insufficient quantity of tissue present in the pre-treatment biopsy (fine needle aspirate). The clinical study report indicates that results were to have been reported separately.
Time Frame	Baseline tumor biopsy
Safety Issue?	No

Analysis Population Description

Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

11. Secondary Outcome Measure:

Measure Title	Plasma Levels of Lactate Dehydrogenase-5 (LDH5)
Measure Description	LDH5 has been shown to be associated with activation of angiogenesis in lung cancer. Circulating levels of LDH5 were to have been measured at each scheduled visit through the post-treatment visit to determine if a correlation with drug effect existed. Levels of LDH5 were measured, but the team determined that greater value was to be derived from transcriptional and plasma biomarker analyses; thus, no analyses were conducted to examine the correlation of LDH5 levels with effects of pazopanib.
Time Frame	Baseline to at least three weeks and at most 8 weeks
Safety Issue?	No

Analysis Population Description

Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

12. Secondary Outcome Measure:

Measure Title	Genetic Variations in Germline DNA
Measure Description	Plasma samples were collected from each consenting participant, generally at baseline, to permit evaluation of the presence or absence of genetic variations in select candidate genes in germline DNA. Analyses that could have been done might have examined the relationship between genetic variants and the safety or tolerability or the efficacy of pazopanib. Analyses have not yet been conducted, but a need to do so may yet be identified. The clinical study report indicated that results, if any, would be reported separately.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

13. Secondary Outcome Measure:

Measure Title	Semiquantitative Levels of Staining in Pre-treatment Tumor Biopsies (e.g. VEGF, VEGFR-1,VEGFR-2).
Measure Description	Analysis not performed as part of study. Appropriate material was not available for analysis.
Time Frame	Entire study interval
Safety Issue?	No

Analysis Population Description

Safety Population: all participants who received at least one dose of pazopanib

Reporting Groups

	Description
Overall Study Arm	

Measured Values

	Overall Study Arm
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

14. Secondary Outcome Measure:

Measure Title	Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins
Measure Description	Baseline and post-therapy plasma samples were obtained from participants. Immunohistochemistry analyses were carried out using a BioPlex 200 machine (Bio-Rad) or by enzyme-linked immunoassays to evaluate levels of angiogenesis-related proteins and other relevant proteins. Post- and pre-treatment changes in cytokines and angiogenic factors in response to pazopanib were analyzed. A negative value indicates that the post-treatment level of the particular target protein was less than the pre-treatment level.
Time Frame	Baseline to at least two weeks and at most 6 weeks
Safety Issue?	No

Analysis Population Description

Safety population: all participants who received at least one dose of pazopanib. Only 33 of 35 subjects had plasma samples from both pre- and post-treatment available for analysis.

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Measured Values

	Pazopanib 800 mg
Number of Participants Analyzed	33
Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins [units: ratio] Median (Inter-Quartile Range)	
Vascular endothelial growth factor receptor	-1.35 (-1.644 to -1.155)
Placental growth factor	18.04 (8.374 to 69.273)
Interferon inducible cytokine	1.60 (1.046 to 2.794)

	Pazopanib 800 mg
Cutaneous T-cell attracting chemokine	1.12 (-1.040 to 1.311)
Stromal cell-derived factor 1	1.08 (-1.013 to 1.100)
Monokine induced by interferon gamma	1.33 (-1.001 to 2.358)
Tumor necrosis factor ligand	1.05 (1.007 to 1.118)
Interferon alpha 2	1.04 (-1.006 to 1.079)
Vascular endothelial growth factor	-1.01 (-1.362 to 2.307)

Statistical Analysis 1 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.01
	Comments	Vascular endothelial growth factor receptor 2 (VEGFR2)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 2 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.01
	Comments	Placental growth factor (PIGF)
	Method	Wilcoxon (Mann-Whitney)

	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 3 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.00024
	Comments	Interferon-inducible cytokine (IP-10)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 4 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0029
	Comments	Cutaneous T-cell attracting chemokine (CTACK)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 5 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No

	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0062
	Comments	Stromal cell-derived factor 1 (SDF-1alpha)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 6 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0069
	Comments	Monokine induced by interferon gamma (MIG)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 7 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0093
	Comments	Tumor necrosis factor ligand (TRAIL)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 8 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.021
	Comments	Interferon alpha 2 (IFN-alpha2)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Statistical Analysis 9 for Ratio of Post- to Pretreatment Expression Levels for Each of the Indicated Pazopanib Target Proteins

Statistical Analysis Overview	Comparison Groups	Pazopanib 800 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.326
	Comments	Vascular endothelial growth factor (VEGF)
	Method	Wilcoxon (Mann-Whitney)
	Comments	Post- versus pretreatment change in levels of cytokines and angiogenic factors in response to pazopanib treatment

Reported Adverse Events

Time Frame	All AEs and SAEs were to be collected and recorded from receipt of first dose of pazopanib until 28 days following cessation of pazopanib, regardless of initiation of new cancer therapy.
Additional Description	[Not specified]

Reporting Groups

	Description
Pazopanib 800 mg	Pazopanib 800 milligrams (mg) (tablets) administered orally once a day for a minimum of 2 and a maximum of 6 weeks

Serious Adverse Events

	Pazopanib 800 mg
	Affected/At Risk (%)
Total	7/35 (20%)
Infections and infestations	
Pneumonia [A] †	1/35 (2.86%)
Psychiatric disorders	
Anxiety [A] †	1/35 (2.86%)
Respiratory, thoracic and mediastinal disorders	
Chylothorax [A] †	1/35 (2.86%)
Cough [A] †	1/35 (2.86%)
Dyspnea [A] †	1/35 (2.86%)
Pulmonary embolism [A] †	1/35 (2.86%)
Vascular disorders	
Hypertension [A] †	1/35 (2.86%)

† 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%

	Pazopanib 800 mg
	Affected/At Risk (%)
Total	33/35 (94.29%)
Gastrointestinal disorders	
Diarrhea [A] †	13/35 (37.14%)

	Pazopanib 800 mg
	Affected/At Risk (%)
Nausea [A] †	12/35 (34.29%)
Vomiting [A] †	4/35 (11.43%)
General disorders	
Asthenia [A] †	3/35 (8.57%)
Fatigue [A] †	13/35 (37.14%)
Infections and infestations	
Urinary tract infection [A] †	2/35 (5.71%)
Investigations	
Alanine Aminotransferase increased [A] †	8/35 (22.86%)
Aspartate aminotransferase increased [A] †	6/35 (17.14%)
Blood alkaline phosphatase increased [A] †	2/35 (5.71%)
Blood thyroid stimulating hormone increased [A] †	2/35 (5.71%)
Metabolism and nutrition disorders	
Anorexia [A] †	2/35 (5.71%)
Musculoskeletal and connective tissue disorders	
Muscle spasms [A] †	2/35 (5.71%)
Pain in extremity [A] †	2/35 (5.71%)
Procedural pain [A] †	2/35 (5.71%)
Nervous system disorders	
Headache [A] †	8/35 (22.86%)
Peripheral sensory neuropathy [A] †	2/35 (5.71%)
Psychiatric disorders	

	Pazopanib 800 mg
	Affected/At Risk (%)
Anxiety [A] †	2/35 (5.71%)
Insomnia [A] †	4/35 (11.43%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] †	2/35 (5.71%)
Dyspnea [A] †	2/35 (5.71%)
Hypoventilation [A] †	2/35 (5.71%)
Skin and subcutaneous tissue disorders	
Alopecia [A] †	2/35 (5.71%)
Erythema [A] †	2/35 (5.71%)
Hair color changes [A] †	5/35 (14.29%)
Rash [A] †	2/35 (5.71%)
Vascular disorders	
Hypertension [A] †	14/35 (40%)

† 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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