

**SCRI GU56: A Phase II Trial of Pazopanib in Patients with Metastatic Renal Cell Carcinoma  
Previously Treated with Sunitinib or Bevacizumab**

*Fast Facts*

**Inclusion Criteria**

1. Male and female patients  $\geq 18$  years of age.
2. All patients must have histologically documented metastatic or unresectable locally recurrent clear cell renal carcinoma. In patients with mixed histologies, any percentage of clear cell histology is acceptable.
3. Patients must have had only one previous targeted agent therapy with either sunitinib or bevacizumab (+/- interferon). Patients must have progressed either during or within 3 months of discontinuing treatment with one of these agents. Patients who stopped either sunitinib or bevacizumab because of unacceptable toxicity are also eligible.
4. Patients may have received one previous regimen containing traditional immunotherapy (interferon, interleukin-2), chemotherapy, or combination chemoimmunotherapy for metastatic disease.
5. Previous nephrectomy is required unless clinically contraindicated (e.g., extensive liver or bone metastases; primary tumor  $< 5$ cm).
6. An ECOG performance status of 0 or 1 (see Appendix A).
7. At least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded) as  $> 20$  mm with conventional techniques, or as  $> 10$  mm with spiral computerized tomography (CT) scan according to the Response Evaluation Criteria in Solid Tumors (RECIST)
8. Absolute neutrophil count (ANC)  $> 1500/\mu\text{L}$ ; platelets  $> 75,000/\mu\text{L}$  (within 7 days prior to study treatment).
9. Adequate liver function as measured by serum bilirubin  $< 1.5$  mg/dL and AST/ALT  $< 2.5$  times upper limit of normal (ULN) (or  $< 5 \times$  ULN in patients with documented liver metastases).
10. Serum creatinine  $< 2.0$  mg/dL.
11. Patients must be able to understand the nature of this study and give written informed consent.

**Exclusion Criteria**

1. Previous treatment with more than one targeted agent, or more than one previous traditional regimen (e.g., chemotherapy, immunotherapy, chemoimmunotherapy).
2. Previous treatment with sorafenib, temsirolimus, everolimus, or other investigational targeted agents.
3. Inability to swallow and retain oral medication.
4. History of other malignancy. Patients who have been disease-free for 5 years, or patients with a history of completely resected non-melanoma skin cancer or successfully treated in situ carcinoma are eligible.
5. Concurrent disease or condition that would make the patient inappropriate for study participation including: (1) any unresolved or unstable serious toxicity from prior administration of another drug, or (2) any serious medical disorder that would interfere with the patient's safety, obtaining informed consent, or compliance with the study.
6. History or clinical evidence of central nervous system (CNS) metastases or leptomeningeal carcinomatosis, except for individuals who have previously treated parenchymal CNS metastases, are asymptomatic, and have had no requirement for steroids or anticonvulsants for  $> 2$  months prior to study enrollment. Routine screening with CNS imaging studies (computed tomography [CT] or magnetic resonance imaging [MRI]) is required only if clinically indicated, or if the patient has a history of CNS metastases.
7. Malabsorption syndrome, disease significantly affecting gastrointestinal function, or resection of the stomach or small bowel.
8. Active peptic ulcer disease, inflammatory bowel disease, or other gastrointestinal condition increasing the risk of perforation.
9. History of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess within 4 weeks prior to beginning therapy.
10. Presence of uncontrolled infection.
11. Concurrent cancer therapy (e.g., chemotherapy, radiation therapy, surgery, immunotherapy, biologic therapy, hormonal therapy, or tumor embolization).
12. Concurrent treatment with an investigational agent or participation in another clinical trial.

13. Use of an investigational anti-cancer drug within 30 days or 5 half-lives, whichever is longer, preceding the first dose of pazopanib.
14. Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to pazopanib.
15. Has taken or is taking prohibited medications listed in Section 5.2.2.
16. Corrected QT interval (QTc) prolongation defined as QTc interval >470 msec.
17. History of any one of the following cardiac conditions within the past 6 months:
  - Cardiac angioplasty or stenting
  - Myocardial infarction
  - Unstable angina
  - History of cerebrovascular accident within the past 6 months
  - Poorly controlled hypertension (systolic blood pressure [SBP] of >150 mmHg, or diastolic blood pressure [DBP] of >90 mmHg).

Note: Initiation or adjustment of antihypertensive 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 24 hours. The mean SBP-DBP values from both BP assessments must be <150/90 mmHg in order for a patient to be eligible for the study. (see Section 4.2.4.)

18. Presence of any non-healing wound, fracture, or ulcer, or the presence of symptomatic peripheral vascular disease.
19. Evidence of bleeding diathesis or coagulopathy.
20. 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.
21. Pregnant or lactating female. All patients of childbearing potential must agree to use adequate contraception for 2 weeks prior to beginning pazopanib, during the entire study, and for 60 days after pazopanib is discontinued.
22. Class III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system (see Appendix B).
23. History of untreated deep venous thrombosis (DVT) within the past 6 months.

#### **Pre-study Parameters**

1. History and physical including BP, heart rate, respiration rate, temperature, ECOG PS, list of concomitant medications
2. CBC with differential, CMP, PT/PTT, UPC ratio or urine dipstick, serum HCG (as applicable)
3. ECG, tumor measurements, CT of chest and abdomen, CT/MRI head as clinically indicated

#### **Treatment**

Pazopanib 800 mg PO daily.

Continue treatment until progression.

Pazopanib provided.