#4684 ASCO 2012

Cleveland Clinic
Taussig Cancer Center

A Phase II Study of Intermittent Sunitinib in Previously Untreated Patients with Metastatic Renal Cell Carcinoma

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Introduction

- Sunitinib is a standard of care first-line treatment in mRCC.
- Balancing acute and chronic treatment toxicity with clinical benefit is challenging.
- Pre-clinical and retrospective clinical data support the concept of treatment breaks without loss of efficacy.[1,2,3]

Hypothesis

- A discontinuation and re-initiation treatment regimen in pts with initial tumor burden reduction to sunitinib is feasible and will lead to disease control with improved tolerance.

Endpoints

Primary Endpoint:

- Determine the feasibility of intermittent sunitinib therapy in pts with mRCC, defined as the proportion of patients eligible for intermittent therapy who receive it.

Secondary Endpoints:

- Objective RR
- PFS
- Toxicity

Statistical Considerations

- An underlying acceptance rate of $\geq$80% is considered necessary in order to accept the intermittent schedule as feasible whereas an acceptance rate $\leq$50% is considered evidence that the intermittent schedule is not feasible.
- A sample size of 20 pts eligible for intermittent therapy (i.e. >10% tumor reduction after 4 cycles of sunitinib) is needed to have 80% power to detect a difference (based on a two-sided exact test with .05 type I error).
- Assuming approximately 2/3 of pts will be eligible for intermittent therapy, at least 30 eligible pts will be accrued.

Patient Selection

Inclusion criteria:

- Advanced RCC with clear cell histology
- Measurable disease per RECIST
- ECOG 0 – 1
- Prior nephrectomy NOT required
- Adequate organ function
- Pts with history of brain metastasis can be enrolled 2 weeks after completion of therapy

Exclusion criteria:

- Prior systemic treatment for advanced RCC
- Hypertension > 160/90 mmHg
- MI, CABG, CVA, TIA, or PE < 6 months.

Treatment Plan

- Sunitinib 50mg 4 weeks on / 2 weeks off
- Supportive care as clinically appropriate
- Standard lab and clinical assessments on day 29 of each cycle
- Intermittent sunitinib dosing will continue until RECIST-defined PD while on sunitinib

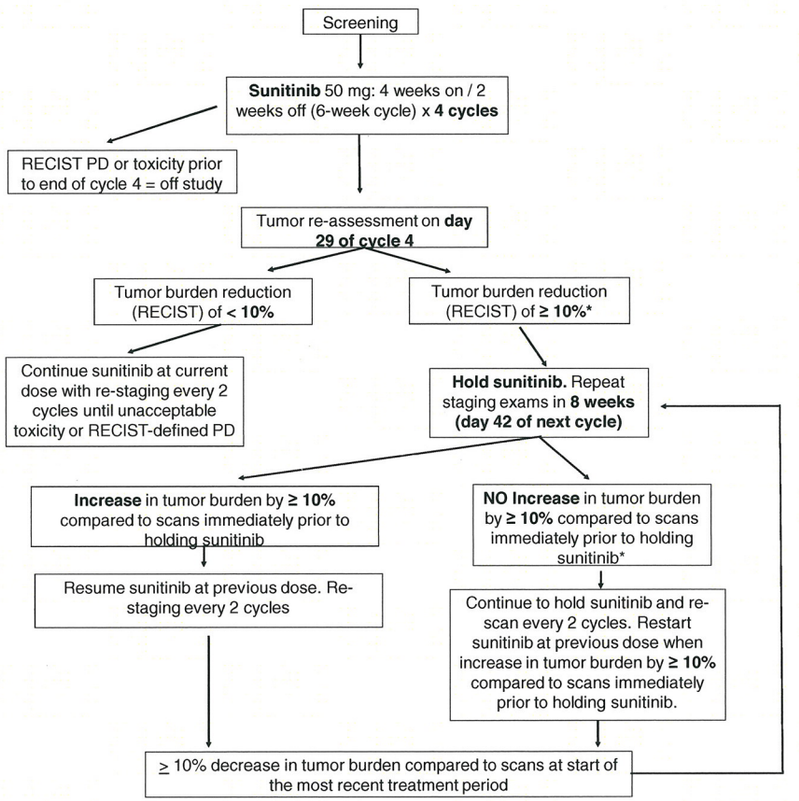
Current Status

- 35 patients have been enrolled
- 12 pts had > 10% tumor burden reduction after Cycle 4 and proceeded to intermittent therapy
- 15 pts had PD or withdrew consent prior to Cycle 4
- 8 pts are within the initial 4 cycles of treatment
- Enrollment is ongoing
- No unexpected toxicities have been observed

References

1. Panka D, Kumar M, Schor-Bardach R, et al. Mechanism of acquired resistance to sorafenib in RCC. *AACR Meeting Abstracts* 2008.
2. Johannsen M, Florcken A, Bex A, et al. Can tyrosine kinase inhibitors be discontinued in patients with metastatic renal cell carcinoma and a complete response to treatment? A multicentre, retrospective analysis. *Eur Urol* 2009.
3. Sadeghi S, Albiges L, Wood LS, et al. Cessation of vascular endothelial growth factor-targeted therapy in patients with metastatic renal cell carcinoma. *Cancer* 2011.

Study Schema



* Assumes non-PD of any/all non-target lesions, otherwise treat as PD