

# Effects of Sunitinib Malate on Metastatic Renal Cell Carcinoma

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## Abstract

A 77 year-old female presented with gross hematuria with no other symptoms. CT scan showed metastatic renal cell carcinoma (mRCC) which spread to the adrenals and IVC. She began treatment with sunitinib malate (Sutent), an oral, multitargeted tyrosine kinase inhibitor. mRCC is a very common and potent disease that is not very treatable. This case report will show how mRCC can be treated and controlled with sunitinib malate.

## INTRODUCTION

A 77 year-old female presents with history of gross hematuria, which occurred 2 months prior for one day. Patient denies any pain, nocturia, or burning, and also states she has no significant GU history. Physical exam was within normal limits and UA was +1 for leukocytes and trace for blood. Further exploration with bladder cystoscopy did not reveal any stones or lesions, and the patient was sent for a CT scan of the abdomen and pelvis

## WORKUP

CT scan w/o contrast revealed a large mass in the lower pole of the right kidney measuring 6.5 x 7.4 cm with metastasis into the right renal vein and proximal inferior vena cava. The patient had metastases to the lungs and both the right and left adrenals measuring 2.6 x 2.6 cm and 2.4 x 1.5 cm, respectively (Figure 1). Right kidney biopsy confirmed the suspicion, showing renal clear cell carcinoma with Fuhrman Nuclear Grade 2.

Figure 1

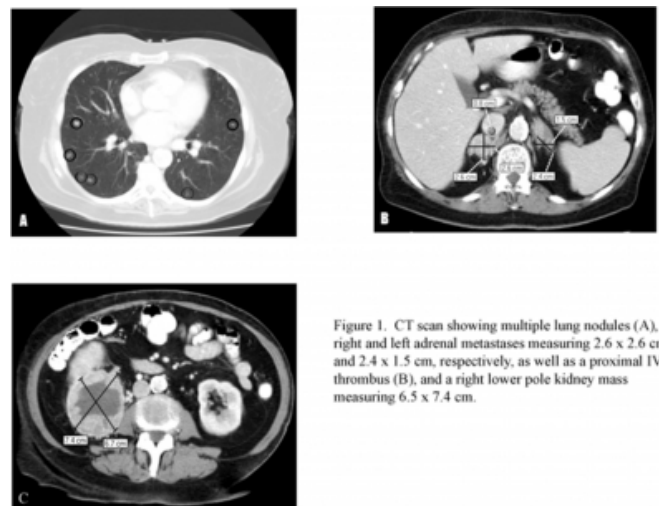


Figure 1. CT scan showing multiple lung nodules (A), right and left adrenal metastases measuring 2.6 x 2.6 cm and 2.4 x 1.5 cm, respectively, as well as a proximal IVC thrombus (B), and a right lower pole kidney mass measuring 6.5 x 7.4 cm.

## DIAGNOSIS

Right renal cell carcinoma extending into the right renal vein and proximal inferior vena cava with metastasis to the lungs and bilateral adrenals. Clinical stage T3b NX M1.

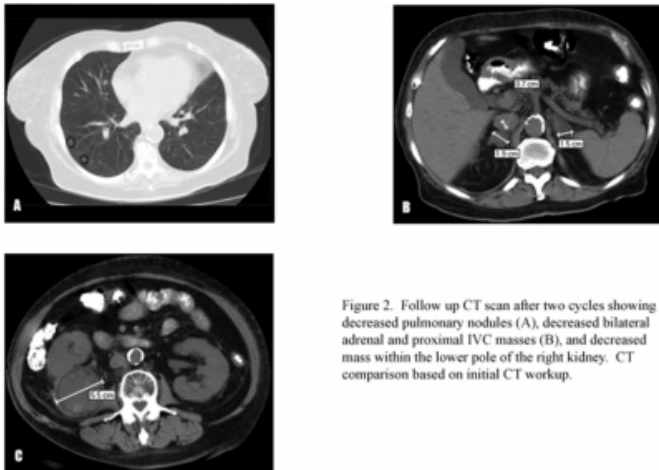
## PLAN AND PROCEDURE

Due to the patients frail condition and severe metastatic disease there was no indication for curative nephrectomy. Therapy was started at 50 mg of Sutent to be taken once daily for four weeks, followed by a two week break, with each cycle lasting six week. After completing two cycles of therapy, a CT scan to evaluate the response to treatment was obtained.

The CT scan showed a decrease in size of the adrenal gland

masses bilaterally and a decreased mass in the lower pole of the right kidney, previously measuring 6.5 cm in diameter, it was now 5.5 cm showing a 15.4% decrease after two cycles. The tumor thrombus within the right renal vein previously measured at 1.4 cm, was now 50% smaller, measuring at 7 mm. The multiple pulmonary nodules were identified as either being equal or decreasing in size (Figure 2).

**Figure 2**



Following three cycles, the patient underwent significant side effects from Sutent including hand-foot syndrome, hypothyroidism, fluid retention, hypertension, and fatigue. All the symptoms appeared during the last week of treatment and disappeared by the time the next cycle started. The fourth cycle of therapy was cut short, after two weeks, due to significant hand-foot syndrome which caused the patient pain during ambulation. The symptoms resolved after stopping therapy.

Therapy was discontinued for 2 weeks, then restarted on a lower dose of Sutent at 37.5 mg.

After five cycles, the patient had complaints of fatigue and right sided flank pain radiating to the groin. CT scan showed stable masses with right hydronephrosis. Sutent was held and the patient underwent right nephrectomy because of symptomatic hydronephrosis.

Due to surgery and discontinuation of therapy, both adrenal glands have increased in size since the previous examination suggesting the presence of metastatic disease (Figure 3).

**Figure 3**

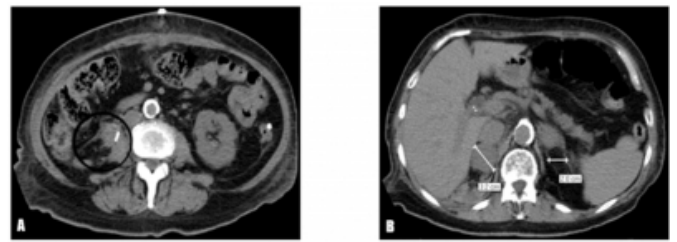


Figure 3. CT scan s/p five cycles of Sutent as well as right kidney nephrectomy (A). Due to surgery and discontinuation of therapy, both the right and left adrenal glands have increased in size, respectively, from 1.9 cm to 3.2 cm and 1.5 to 2.0 cm in diameter since the previous examination (B)

Therapy was continued after surgery and at the completion of the seventh cycle the patient had been on Sutent therapy for one year. CT scan showed a decrease in size of the bilateral adrenal masses as compared to postop. The right adrenal mass had decreased back down from 3.2 cm to 1.9 cm, while the left adrenal lesion had decreased from 2.0 to 1.2 cm. There was no significant change in the lung nodules and the thrombus in the IVC had remained stable (Figure 4).

**Figure 4**

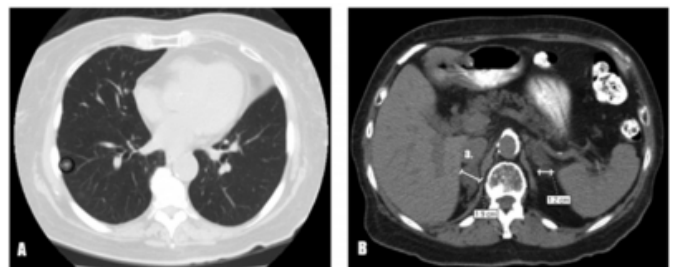


Figure 4. CT scan after seven cycles of therapy showing a decrease in size of the adrenal masses as compared to postop. The right adrenal mass decreased back down to 1.9 cm and the left adrenal lesion had decreased from 2.0 to 1.2 cm (B). There was no significant change in the lung nodules (A) and the thrombus in the IVC had remained stable (a).

Sutent effectively decreased the size of the tumors. Tumor mass in the lower right pole decreased 15.4%, the right adrenal mass underwent a 26% decrease, the left adrenal mass had a 50% decrease, the IVC thrombus initially decreased 50% after two cycles and now remains stable along with the lung nodules.

The patient has started on her tenth cycle of therapy and is doing very well. None of the masses have increased in size and the patient no longer has side effects to the medication.

## DISCUSSION

Metastatic renal cell carcinoma is the most common and one of most resistant tumors in urology with only a less than 10% survival rate for 5 years <sup>1,2</sup>. It is generally characterized by a lack of early warning signs, diverse clinical manifestations, and resistance to radiation and chemotherapy

Over the past few decades there has seemed to be an increase in the incidence of all stages of RCC<sup>3</sup>. It has the reputation of leading to poor prognoses as most therapy ideas seem to have no influence on this disease. Recently, it has been shown that RCC is caused by a loss in the von Hippel Lindau (VHL) tumor suppressor gene activity. A mutation in the VHL gene can cause an increase in hypoxia inducible factor-1 $\alpha$ , which in turn can cause an increase in both VEGF and PDGF<sup>2,5,6,7,8</sup>.

Currently, the treatment opportunities for metastatic renal cell carcinoma are very limited and there is dire need for a new therapy. Sunitinib malate is an oral, multitargeted tyrosine kinase inhibitor that specifically inhibits vascular endothelial growth factor receptors, platelet-derived growth factor receptors, and other tyrosine protein kinases<sup>2</sup>. Due to its affinity for VEGF and PDGF receptors, Sutent is able to effectively work on renal cell carcinoma.

Recently, the first Phase III study proved that Sutent was more efficacious compared to interferon- $\alpha$ . The trial showed that 28% of patients on Sutent had significant tumor shrinkage compared with only 5% of patients who received interferon- $\alpha$ . These results proved that Sutent should now be the gold standard in care for patients with mRCC<sup>9</sup>. Patients receiving sunitinib also reported a significantly better quality of life than those treated with interferon- $\alpha$ <sup>10</sup>.

### References

1. Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. *N Engl J Med*. 1996; 335:865-875.
2. Ronnen EA, Kondagunta GV, Ginsberg MS, et al. Long-term Response with Sunitinib for Metastatic Renal Cell Carcinoma. *Journal of Urology* 2006; 672:19-20.
3. Motzer RJ, Rini BI, Bukowski RM, et al. Sunitinib in Patients with Metastatic Renal Cell Carcinoma. *JAMA* 2006; 295:2516-2524.
4. Hock LM, Lynch J, Balaji KC. Increasing Incidence of All Stages of Kidney Cancer in the Last 2 Decades in the United States: An Analysis of Surveillance, Epidemiology, and End Results Program data. *Journal of Urology* 2002; 167:57.
5. Sosman JA. Targeting of the VHL-Hypoxia-Inducible Factor-Hypoxia-Induced Gene Pathway for Renal Cell Carcinoma Therapy. *J Am Soc Nephrol* 2003; 14:2695-2702.
6. Gunaratnam L, Morley M, Franovic A, et al. Hypoxia Inducible Factor Activates the Transforming Growth Factor-Alpha/Epidermal Growth Factor Receptor Growth Stimulatory Pathway in VHL (-/-) Renal Cell Carcinomas. *J Biol Chem* 2003; 278:44966-44974.
7. Motzer RJ, Michaelson MD, Redman BG, et al. Activity of SU11248, a Multitargeted Inhibitor of Vascular Endothelial Growth Factor Receptor and Platelet-Derived Growth Factor Receptor in Patients with Metastatic Renal Cell Carcinoma. *J Clin Oncol* 2006; 24:16-24.
8. Kenck C, Wilhelm M, Bugert P, et al. Mutation of the VHL Gene is Associated Exclusively with the Development of Non-Papillary Renal Cell Carcinomas. *J Pathol* 1996; 179:157-161.
9. Motzer RJ, Hutson TE, Tomczak P, et al. Phase III Randomized Trial of Sunitinib Malate (SU11248) Versus Interferon-Alpha (IFN- $\alpha$ ) As First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma (mRCC). *J Clin Oncol*, 2006 ASCO Annual Meeting Proceedings Part I. Vol 24, No. 18S (June 20 Supplement), 2006: LBA3
10. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib Versus Interferon Alfa in Metastatic Renal-Cell Carcinoma. *N Engl J Med* 2007; 356(2):115-124.

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