



# Newsletter of the DF/HCC Renal Cancer Program

[www.dfhcc.harvard.edu/renalcancer](http://www.dfhcc.harvard.edu/renalcancer)

Spring 2006

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- *Adjuvant Trial*
- *Resistance Trial*



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## Regional Kidney Cancer Symposium and 3rd Annual Kidney Cancer Mini-Symposium:

By Michael Atkins, MD

The DF/HCC Renal Cancer Program held two exciting, cutting-edge educational activities this spring. The initial event, a full day symposium focused solely on kidney cancer, was held on Friday, April 7th at the Copley Marriott Hotel. The program consisted of 16 lectures by leaders within the DF/HCC renal cancer community covering the areas of kidney cancer biology, therapy, treatment selection and treatment monitoring. The major goal was to present current information regarding the various new anti-angiogenic and targeted agents in a balanced way, and to discuss how, when and in whom to use them. With coverage of interleukin 2, sorafenib, sunitinib, bevacizumab and temsirolimus, the symposium attempted to not only cover current data, but also provide a framework for interpreting the results of studies using these agents that were to be presented at the ASCO Annual meeting held in June, 2006 (see page 3). The Symposium was attended by over 80 physicians, nurses and pharmaceutical representatives from around New England making for lively question and answer periods following each lecture and informative panel discussions. As a bonus, Arlene Hsu, RN, from BIDMC and her colleagues Beverly Spicer, RN, BSN, from MGH and Judith Prisky, RN, BSN, Laurie Appleby, APRN, and Stephanie Morrissey, RN, from DFCI, led a Nursing Breakout Session focused on clinical management issues with the new agents. The meeting was supported by generous donations from Chiron, Schering-Plough, Pfizer, Bayer-Onyx and Genentech with CME accreditation provided by Harvard Medical School and CE accreditation provided by ONS.

On April 27, 2006, the DF/HCC Renal Cancer Program hosted its 3rd Annual Kidney Cancer Mini-Symposium for the DF/HCC community. This year's mini-symposium featured lectures from 4 speakers—a medical oncologist, urologist, pediatrician and radiologist—one each from the West Coast, East Coast, North and South. The speakers are listed at right.

The mini-symposium was well attended and the varied topics contributed to a very informative afternoon and a lively exchange of ideas. It is anticipated that several translational research projects will result directly from the scientific interactions fostered by this event.

### 3rd Annual Kidney Cancer Mini-Symposium

**Robert Figlin, MD, FACP**

Medicine and Urology, David Geffen School of Medicine at UCLA  
*"Protein Expression Profiles in Renal Cell Carcinoma: Staging, Prognosis, and Patient Selection for Clinical Trials"*

**Augusto Ochoa, MD**

Stanley Scott Cancer Center, Louisiana State University Health Sciences Center  
*"The role of arginase, prostaglandins and immature myeloid cells in renal cancer-induced immuno-suppression"*

**Eugene Kwon, MD**

Urology and Immunology, Mayo Comprehensive Cancer Center  
*"The role of B7H1 as a prognostic factor and a potential therapeutic target in renal cancer"*

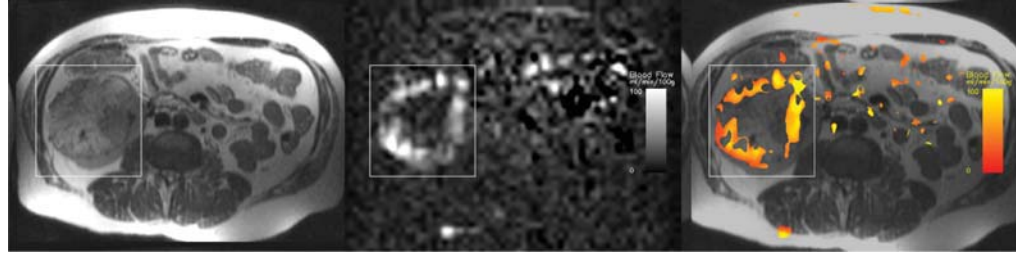
**Mark Rosen, MD, PhD**

Radiology, University of Pennsylvania Medical Center  
*"Dynamic contrast enhanced MRI (DCE-MRI) for non-invasive vascular assessment of Renal Cell Carcinoma: Imaging phenotypes and response assessment to targeted therapies"*

# Monitoring Core

By Vikas Sukhatme, MD, PhD

The **Monitoring Core** is an integral infra-structural part of the Renal SPORE and serves the translational needs of all of the projects. It was created with multiple components in order to provide maximal flexibility in serving these needs. It currently has three components: angiogenesis, immunologic and imaging monitoring. For each of these areas there are a number of “assays” that are made available to SPORE investigators. For example, the angiogenesis monitoring core’s main function is to devise methods to gauge the efficacy of anti-angiogenic therapy for renal cancer via the development of non-invasive assays. Given the recent approval of sorafenib and sunitinib for RCC, there is a pressing need to be able to predict responders and relapsers especially prior to conventional imaging studies. Current studies are aimed at collecting, processing, and cataloguing blood of patients on antiangiogenic therapy and developing methods to measure plasma cytokines, circulating endothelial cells, and



T2-weighted images (left) and perfusion images (middle and right) obtained with Arterial Spin Labeling (ASL) in a patient with poorly differentiated renal cell carcinoma. The gray scale perfusion image (middle column) shows perfusion in tumor but the background suppression erased all anatomical information. The image to the right shows color coded perfusion mapping applied to the T2-weighted images for a simultaneous display of the functional and morphological information. The ASL technique is useful in monitoring response to a variety of treatments, particularly for anti-angiogenic therapies.

patient blood gene expression to answer these questions.

The imaging core has a number of novel imaging capabilities, largely MR based, for the same purpose and has some promising early data—see figure above (from Drs. Rofsky and Alsop). The core also provides investigators with a centralized method for obtaining standardized measurements of radiological scans (CT, MR and PET) to

evaluate tumor response for clinical trials.

Finally, the immunologic core assesses a number of immune patient functions, such as dendritic cells functions and antigen specific T cells. It is becoming increasingly clear that immune based therapies can affect the action or amount of angiogenic cytokines, so that the function of these cores has started to complement each other.

## Image-Guided Radiofrequency Ablation for Renal Cell Carcinoma

By S. Nahum Goldberg, MD

Although partial nephrectomy is the established treatment for small renal cancers, less invasive image-guided procedures have emerged. One of these techniques, radiofrequency (RF) tumor ablation (i.e., coagulating tumor using short duration heating [less than 15 minutes] by directly applying temperatures over 50°C via needle electrodes) is being incorporated as a clinical tool for the treatment of renal cell carcinoma. RF ablation has been used to treat focal liver tumors where potential benefits of this outpatient thermal therapy include reduced morbidity and mortality compared to standard surgical resection and the ability to treat non-surgical patients. More recently, this technique has been introduced to treat focal renal tumors, particularly incidental < 3 cm lesions in the elderly and those with co-morbid conditions. Other uses have included treatment in patients with Von-Hippel-Lindau syndrome and other diseases that predispose towards multiple renal carcinomas where maximum preservation of renal function is desired, and focal regions of metastatic disease. Additionally, based upon our demonstration of the complementary interaction between RF ablation and antiangiogenic therapy in the laboratory, we are recruiting patients to clinical



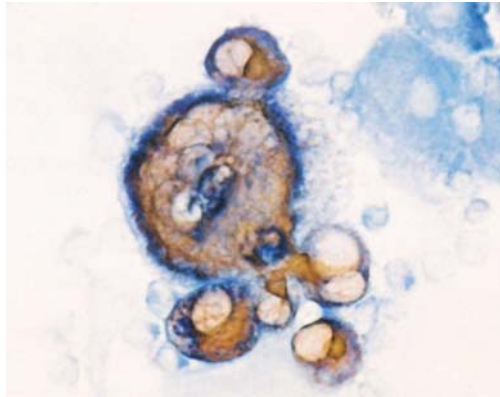
RF ablation of a centrally located renal tumor measuring 4.5 by 3.5 cm (left). Before treatment, tumor (black arrow) reveals contrast enhancement on CT imaging (center). RF ablation was performed using an internally cooled cluster electrode (black arrow) for 30 minutes (separated into 4 treatments). Gas vapor is seen (arrowheads) along the needle shaft, indicating the intensity of heating and tissue vaporization (right). The 18-month follow-up reveals no tumor enhancement, suggesting complete treatment (white arrow). Bright enhancement of the collecting system (black arrow) reveals intact functional calyces after treatment. Perirenal fat necrosis is also observed (arrowheads).

cal trials combining RF ablation with sorafenib. These trials will be open to patients who have failed systemic antiangiogenic therapy, and those with stage IV disease undergoing debulking nephrectomy.

# Novel Cancer Vaccine for Patients with Metastatic Renal Carcinoma

By David Avigan, MD

We have designed a cancer vaccine model in which patient-derived tumor cells are isolated and fused to potent immune stimulating cells known as dendritic cells (DCs). In this way, a broad array of tumor antigens is presented in the context of the powerful immune machinery of the DCs. In pre-clinical studies, vaccination with fusion cells stimulated anti-tumor immunity and was effective in eradicating established metastatic disease. We have conducted clinical studies in patients with renal carcinoma in which vaccination was well tolerated and associated with clinical and immunologic responses in a subset of patients. One potential issue limiting vaccine efficacy is that tumor-bearing patients exhibit immune deficiencies resulting from their disease. In contrast, debulking nephrectomy may enhance patient immunity by reducing the inhibitory influence of the malignant cells. In the current trial, patients with metastatic renal carcinoma undergoing therapeutic nephrectomy will undergo vaccination with renal carcinoma cells fused with autologous DCs. The tumor cells will be obtained from the nephrectomy specimen and then fused with DCs that have been generated in our clinical immunotherapy facility. We will be examining the ability of vaccination to stimulate anti-tumor immune responses as well as disease regression. We will also be examining the relationship between the immune status of patients post-nephrectomy with vaccine response.



## Renal Cancer Research Featured at ASCO 2006

The results of two large phase III trials involving the use of targeted and anti-angiogenic agents in previously untreated patients with advanced renal cancer were presented at the recent ASCO meeting in Atlanta. The first trial, presented by Dr. Robert Motzer from Memorial Sloan Kettering Cancer Institute, involved a randomized comparison of sunitinib and interferon alpha in patients with largely good and intermediate prognosis renal cancer. This trial involving 750 patients showed that sunitinib produced a response rate of 31% and a median progression free survival of 11 months compared to 5 months and 6% for interferon. These highly significant differences were produced without significant increase in toxicity. As yet no signifi-

cant difference in overall survival has been observed, although follow-up is early. The second study, presented by Dr. Gary Hudes from the Fox Chase Cancer Center, involved a three-arm comparison of temsirolimus, the combination of temsirolimus and interferon and interferon alone in patients with poor prognostic clinical features. This study involved 600 patients and showed near 50% prolongation in median survival for the temsirolimus alone arm compared to interferon. The temsirolimus plus interferon arm was not significantly different than interferon alone, suggesting that the reduction in temsirolimus dose in the combination regimen in order to accommodate the side effects of interferon may have compromised efficacy. In discussing these studies

## Awards/In the News

Rupal Bhatt, MD PhD, a 4th Year Postdoctoral Fellow in Dr. Vikas Sukhatme's lab, has received 3 separate awards over the past year: AACR Clinical/Translational Fellowship Award; ASCO Young Investigator's Award; CTIP Young Investigator's Award

## Research Funding Opportunities

**DF/HCC Renal Cancer SPORE Career Development Awards – RFA**

Due Date: 6/26/06

**DF/HCC Renal Cancer SPORE Developmental Project Awards – RFA**

Due Date: 6/26/06

## Calendar

July 16-19, 2006

**14th Annual SPORE Investigators' Workshop**  
Baltimore Marriott Waterfront Hotel,  
Baltimore, MD

October 26-28, 2006

**7th Biennial Medical Symposium on VHL**  
London, Ontario, Canada  
Sponsored by the VHL Family Alliance:  
[www.vhl.org](http://www.vhl.org)

## Patient Connections

A volunteer group of patients, the *Kidney Cancer Patient-to-Patient Network*, is available to provide support to newly diagnosed patients and their families. For more information, contact Susan Graham-McLoughlin, clinical liaison, at 617-667-1930.

at ASCO, Dr. Michael Atkins commented that these studies establish that "both sunitinib and temsirolimus are considerably more active than single agent interferon as first-line treatment for advanced renal cancer. However, as agents produced few complete responses and required continued administration for efficacy, consideration needed to be given as to which of the various active agents should be given first, when therapy should be initiated, and who should receive which treatment. In addition, the treatment of patients whose disease has progressed on VEGF inhibitor therapy remains a complete black box." Many of these important questions are the focus of ongoing studies within the DF/HCC Renal Cancer Program.



**DF/HCC Renal Cancer Program Members:**

- Seth Leo Alper, BIDMC
- Len Appleman, DFCI
- Michael B. Atkins, BIDMC
- David E. Avigan, BIDMC
- Joseph V. Bonventre, MGH
- Deborah Burstein, BIDMC
- Eunyoung Cho, BWH
- Sandra L. Dabora, BWH
- Douglas Dahl, MGH
- S. Nahum Goldberg, BIDMC
- Daniel A. Haber, MGH
- William Hahn, DFCI
- David P. Harrington, DFCI
- Othon Iliopoulos, MGH
- William G. Kaelin, DFCI
- Donald W. Kufe, DFCI
- Towia Aron Libermann, BIDMC
- Kevin R. Loughlin, BWH
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- Vikas P. Sukhatme, BIDMC
- Patrick Wen, BWH

This newsletter was supported in part by  
Chiron Corporation, Genentech, Inc., and Onyx Pharmaceuticals.

Next edition:  
September 2006

**NCI** **DANA-FARBER/HARVARD CANCER CENTER**  
**CCC** A Comprehensive Cancer Center  
Designated by the National Cancer Institute

# Newsletter of the DF/HCC Renal Cancer Program



## Current Clinical Trials *(for complete list visit our web site at [www.dfhcc.harvard.edu/renalcancer](http://www.dfhcc.harvard.edu/renalcancer))*

### Advanced Disease

- A Phase I/II Trial of Sorafenib in Combination with Bevacizumab in Patients with Advanced Renal Cancer. Investigator initiated CTEP sponsored trial of a VEGFR/PDGFR inhibitor (Sorafenib) and a VEGF neutralizing antibody (Avastin) in patients with metastatic RCC. Patients receive escalating doses of these targeted therapies in the Phase I portion of the study.
- Vaccination of Patients with Renal Cancer with Dendritic Cell/Tumor Fusions and GM-CSF. A phase II trial for untreated patients who present with metastatic disease and primary tumor in place. They receive a series of vaccinations using fusions of autologous dendritic cells and tumor cells obtained from the debulking nephrectomy specimen and GM-CSF. (SPORE Project 5).

- A Phase I Study of Sutent and Gemcitabine in Patients with Advanced Solid Tumors. Industry sponsored, dose escalation trial of both agents, open to non-clear cell histologies.
- A Phase 2 Multi-Center, Randomized, Open-Label Study of Two Dose Levels of IMOxine™ (HYB2055 for Injection) in Patients with Metastatic or Locally Recurrent Clear Cell Renal Carcinoma. Industry sponsored, Phase II Trial, first and second line. Toll receptor like agonist (TLR-9), given by subcutaneous injection, weekly for up to 24 weeks.
- A Phase II, investigator initiated, multicenter trial of High-Dose IL-2 and Bevacizumab that will test the safety and efficacy of this combination therapy in untreated patients with metastatic clear cell RCC.

### Adjuvant Therapy

- A randomized double blind phase III Study to evaluate adjuvant cG250 treatment versus placebo in patients with clear cell RCC and high risk of recurrence. Industry sponsored, international study of monoclonal antibody therapy to cG250 (Carbonic Anhydrase IX) following nephrectomy for patients in three high risk categories (T3b, T3c or T4 + N0M0, any T and N+ disease, T1b, T2 or T3a + MVI and Grade > 3).

### Laboratory Correlates

- Analysis of Discarded Tissue in Patients with Renal Cell Carcinoma undergoing either nephrectomy or resection of metastatic disease. Tumor tissue is stored in our Tissue Bank to be analyzed by gene expression profiling and various immunohistochemical and RT-PCR techniques in an effort to discover new prognostic factors, predictors of response and resistance, and new therapeutic targets.
- Collection of Specimen and Clinical Data From Patients with Renal Cell Carcinoma Tissue banking and database protocol (SPORE PATH CORE).

#### Contact Information/Donations:

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