Outcomes in Oncology

Ochsner Cancer Institute's Report to Physicians
June 2014

ochsner.org/cancer

Rodney J. Landreneau M.D.
Medical Director,
Ochsner Cancer Institute

Treatment Advances in Kidney Cancer

Dear Physicians,
In this issue of Ochsner Cancer Institute's "Outcomes in Oncology" newsletter, Dr. Ryan Hedgepeth, of Ochsner's Urology Department discusses the important problem of renal cell carcinoma in our country today. This is a particularly prevalent cancer in our area. As noted by Dr. Hedgepeth, over 64,000 patients will be diagnosed with kidney cancer in the United States in 2014. The good news is that the majority of patients can be successfully treated.

The Ochsner Cancer Institute is one of the leading clinical and urologic cancer research groups in the South. The team of urologic cancer surgeons, medical oncologists, radiation oncologists and their cancer nursing staffs are leading the way in the management of renal carcinoma. Exciting clinical investigative treatment protocols and surgical innovations led by this cancer team for the renal cancer patient are detailed in this message by Dr. Hedgepeth. This "Home Team" of specialists at the Gayle and Tom Benson Cancer Center of the Ochsner Cancer Institute is a great resource to the urologic cancer patient in Louisiana and the Gulf South.

As our stated mission, the purpose of the "Outcomes in Oncology" newsletter series is to provide the health care professionals of the Gulf South with timely and accurate accounts of important cancer problems that they may encounter in their daily practice.

Thank you for participating in this important educational effort provided by the Ochsner Cancer Institute.
Sincerely,

Rodney J. Landreneau, M.D.
Medical Director, Ochsner Cancer Institute

Urologic Cancer Team:

Urology
Stephen Bardot, M.D.
Ryan Hedgepeth, M.D., M.S.
M'Liss Hudson, M.D.

Radiation Oncology
Troy Scroggins, M.D.

Medical Oncology
Zoe Larned, M.D.
Marc Matrana, M.D.

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The Evolving Treatment of Kidney Cancer: A Multimodal Strategy

The Problem of Kidney Cancer

The American Cancer Society estimates that in 2014 approximately 64,000 people will be diagnosed with kidney cancer and almost 14,000 patients will die of their disease.[1] The majority of these patients will present with clear cell renal cell carcinoma (RCC), the most common type of kidney cancer. While the widespread use of abdominal imaging in the last 30 years has led to earlier diagnosis, 20 to 30 percent of RCC patients still present with metastatic disease. About the same percentage of patients who initially have curative surgery will develop metastatic disease during follow-up surveillance.[2] In the past, patients with advanced or metastatic kidney cancer have generally been considered incurable and most succumb to the cancer. Recently, however, advances in our understanding of RCC have led to new thinking in the role of surgery, targeted therapy, and immunotherapy in fighting this malignancy. Patients have seen increased survival times that highlight the need for multi-disciplinary treatment.

Advances in Surgery Improve Patient Outcomes

For several years, centers of excellence across the country such as Ochsner have been taking open and laparoscopic techniques for treating localized kidney cancer and refining them further using robotic technology. While many treatment guidelines recommend partial nephrectomy for small to moderate size tumors, these techniques have not seen widespread use, possibly due to the technical skills needed to perform them[3] **(Image 1).** Patient survival, however, has been clearly linked to residual kidney function. Patients who undergo partial nephrectomy for kidney cancer are noted to have superior survival over those who undergo radical nephrectomy.[4]

Ryan Hedgepeth, M.D.
Director, Urologic Oncology and Robotics

While surgery offers patients with localized kidney cancer an excellent chance of cure, its role in metastatic disease has rapidly broadened. Traditionally, patients with metastatic disease were offered surgery only for palliative purposes because they were considered incurable **(Image 2).** Recent data, however, has shown prolonged survival times for patients with good performance status (ECOG 0,1) who undergo cytoreductive surgery.[5,6] The advantages of robotic and laparoscopic surgical approaches has made these surgeries more palatable for patients by facilitating larger tumor removal through smaller incisions, decreasing morbidity and convalescence, and getting patients back to their normal lives more quickly.[7]

Ochsner surgeons at the Center for Urologic Oncology are endeavoring to improve on emerging surgical principles for patients with all stages of disease. The use of real time tumor fluorescence **(image 3)**, a novel non-clamping (zero ischemia) technique for robotic partial nephrectomy, and the judicious use of ablative tumor techniques are improving cancer control and kidney function outcomes for patient with localized disease. For patients with metastatic disease, our surgeons are performing minimally invasive cytoreductive nephrectomies on larger tumors than ever before with less morbidity for patients.

The Advent of Targeted Therapy

Defining the mechanisms of cancer growth and spread as well as genetic sub-typing of kidney cancer has allowed for the identification of key parts of the process that can be targeted.[8] Several genetic changes associated with kidney cancer have been shown to lead to increases in hypoxia inducible factors and vascular endothelial growth factor (VEGF) – mechanisms that increase tumor angiogenesis and proliferation.[9] Since 2005, a steady stream of new drugs targeting these mechanisms of growth has led to longer survival for patients with metastatic disease[10] **(Image 4).** While not capable of reversing the course of the cancer, these targeted therapies do appear to work synergistically with surgical removal of the primary tumor to give selected patients even more improved survival.[11]

Harnessing the Body's Defenses - Immunotherapy

Previous attempts to harness the body's own defenses have had limited success in kidney cancer. Interleukin therapy is the only potential cure for metastatic disease but it is costly, carries significant

risk, and only about 10 percent of patients have a complete response to therapy. Of those who respond, however, 60 to 70 percent will have a durable cure.[12] Despite limited success, these facts highlight the role that the immune system may play in defeating this disease. The contribution of AIDS research in the 1990s to understanding the body's intrinsic defense mechanisms has now led to a renewed push into immunotherapy. It is now clear that kidney cancer can temper anticancer immune response at various signaling checkpoints and new drugs are being developed to exploit this critical step in immune regulation.[13] Clinical trials to harness the power of the body's dendritic cells, T-cells, and complex coordinated response to antigen are now underway. The Benson Cancer Center is participating in several of these clinical trials that can offer patients a new way to fight kidney cancer. Perhaps more importantly, a team of Ochsner scientists and clinicians are working together to characterize and identify markers of kidney cancer tumor stem cells. These cells are thought to be responsible for metastatic spread, the cancer's ability to avoid immune surveillance, as well as their notorious potential to develop resistance to systemic treatments **(Image 5).**

Patients First – Science, Safety, and Outcomes

Alton Ochsner's scientific endeavor linking smoking and lung cancer and subsequent advocacy for patient health serves as the role model for scientific patient advocacy. Over the last year the Center for Urologic Oncology at the Benson Cancer Center has developed a number of initiatives meant to benefit our patients' safety and outcome. In March 2014, we completed a comprehensive look at patients with kidney cancer as they move through the surgery and recovery process. This led us to develop our own guidelines for recovery based on all of the available data both within our own hospital and in the scientific literature. We consider these pathways each to be a best practice approach to patient care and are now implementing them in order to minimize variation in care and improve patient safety and health **(Image 6).** We will be adding new components to our pathways in the coming year, such as systematically addressing the psychological and emotional needs of each patient in order to ensure support is offered for patients and families in need. Finally, there is a strong need for cancer survivorship programs that address patient needs long after the cancer treatments are completed.[14] The Center for Urologic Oncology is currently developing a comprehensive survivorship program in all of our urologic cancers to improve patients' long term outcomes, foster patients' confidence, and increase the quality of life associated with an increase quantity of life after treatment.

Conclusions: Rewriting the Treatment Paradigm

Advances in surgical technique and the success of targeted therapy have transformed the treatment paradigm for kidney cancer and improved survival. A coordinated multi-disciplinary treatment effort is necessary to achieve optimal cancer survival. Exciting new approaches to treatment, based on our understanding of tumor biology and immune response, are evolving rapidly. Comprehensive treatment and survivorship programs are being developed to optimize patient survival and outcomes.

Questions or more information

Ryan Hedgepeth, M.D. | 504-842-7721

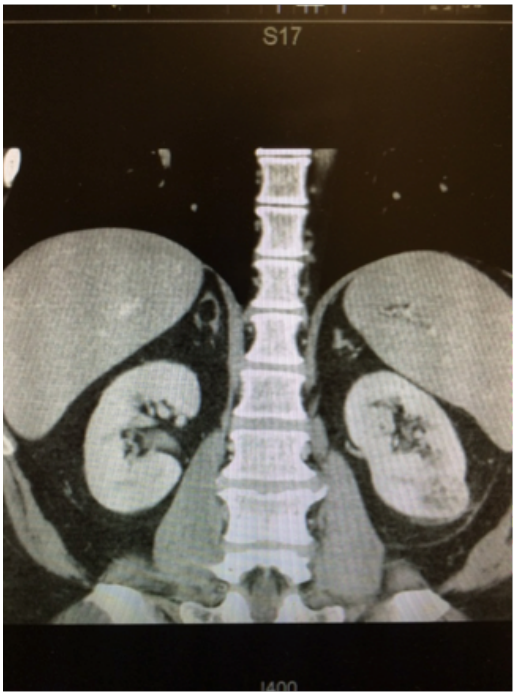
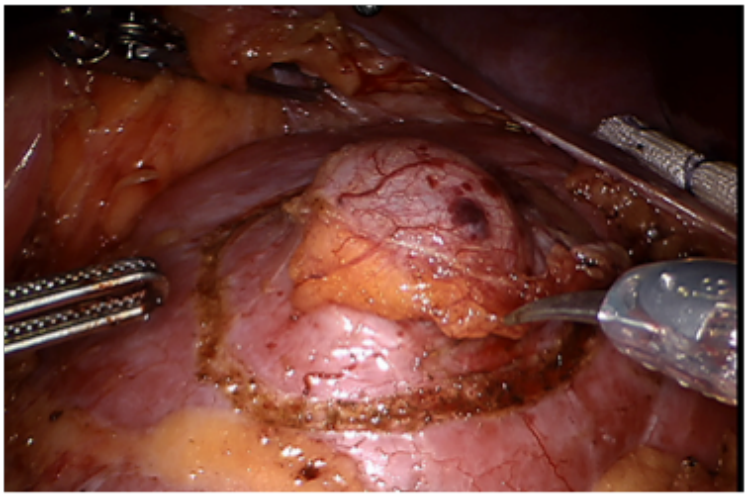


Image 1 – Small renal mass in the inferior pole of the left kidney – survival data support the use of a partial nephrectomy instead of radical nephrectomy.

Image 2 – Large left renal mass with bilateral adrenal metastase- survival data support the use of a cytoreductive radical nephrectomy in patients with good performance status.



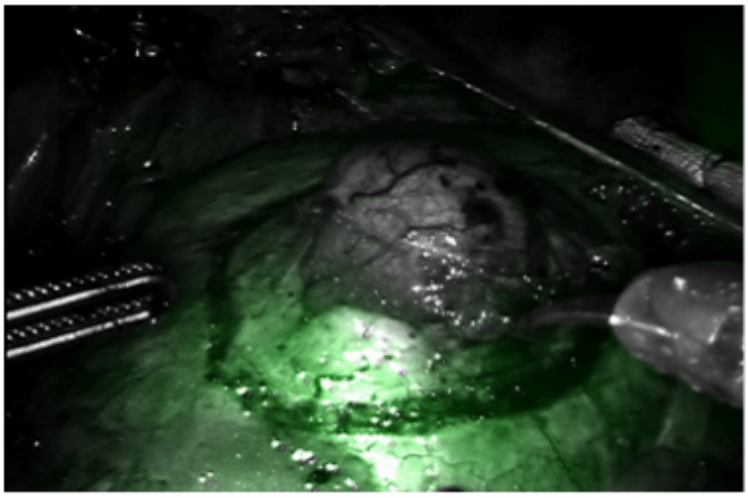


Image 3 – Tumor fluorescence can aid in identifying and resecting all of a kidney tumor during robotic laparoscopic surgery. (Image used with permission)

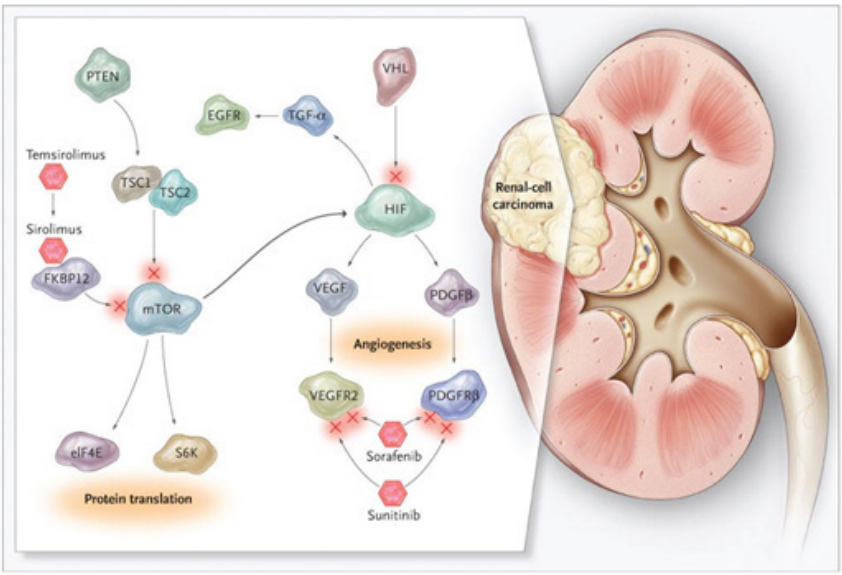


Image 4 – Schematic representation of the pathway used by kidney cancer cells to increase angiogenesis and tumor proliferation. Different points in this process are damaged by targeted therapy (noted by X's) in the medical treatment of kidney cancer.

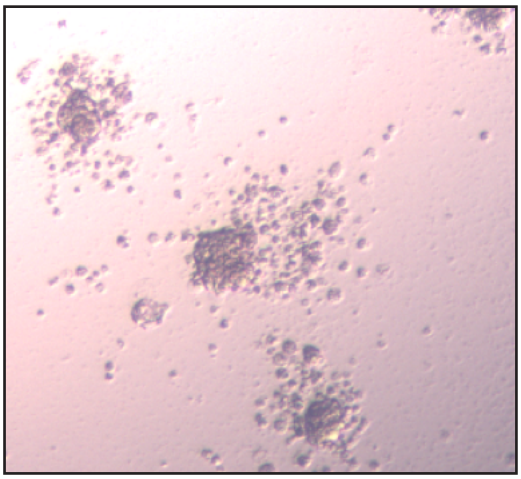


Image 5 – Tumor stem cells are thought to be responsible for metastasis, avoidance of immune surveillance, and development of resistance to treatments. Here tumor stem cells are seen growing in spheres through novel process. Research to identify markers to target these cells is currently underway in the Benson Cancer Center at the Ochsner Clinic.

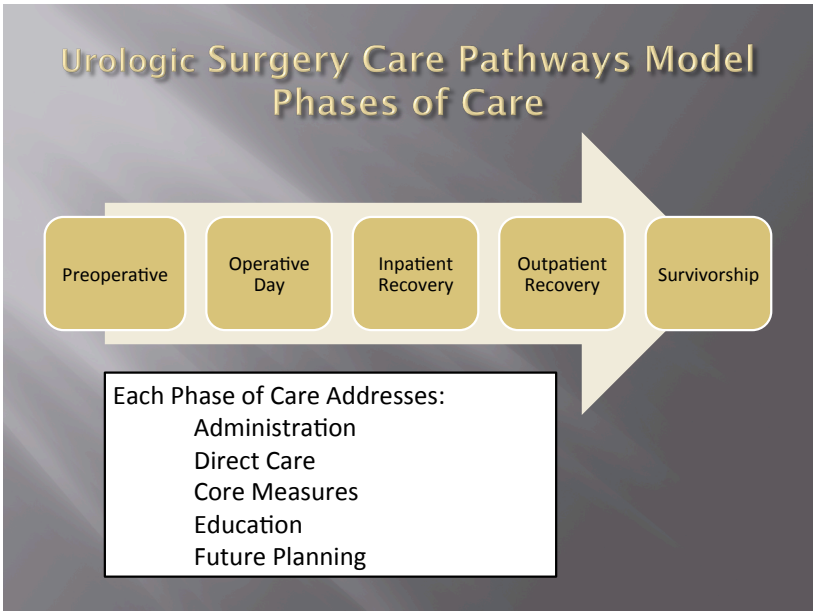


Image 6 – Conceptual Model of the Urologic Surgery Care Pathways Program guides patients through different phases of care and into cancer survivorship by addressing key needs at each phase.

Upcoming "Outcomes in Oncology" Topics:

July: Dermatologic Oncology
August: Colorectal Oncology
September: Hepatobiliary Malignancy
October: Breast Cancer
November: Gynecologic Oncology
December: Neurooncology

Upcoming CME Oncology Activities:

June 27, 2014
Pulmonary Hypertension Conference
Brent House Conference Center, New Orleans, LA

July 25-26, 2014
10th Annual Update in Pediatrics
Brent House Conference Center, New Orleans, Louisiana

July 31 - August 2, 2014
Piedmont Society of Colon & Rectal Surgeons - Summer 2014
Ritz Carlton, Amelia Island, FL

Information and registration for all conferences are available on our website at ochsner.org/cme

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Ochsner Health System

1514 Jefferson Highway
New Orleans, LA 70121

Important Renal Cancer Treatment Protocols at Ochsner Cancer Institute

NCT 01582672 ADAPT:	Phase 3 Trial of Autologous Dendritic Cell Immunotherapy (AGS-003) Plus Standard Treatment of Advanced Renal Cell Carcinoma (RCC) (ADAPT)
S0931 EVEREST:	EVErolimus for Renal Cancer Ensuing Surgical Therapy, A Phase III Study
IRB 2011.222.A	Understanding the Microenvironment of Cancer Stem Cells in Renal Cell Carcinoma

To refer a patient to our Urologic Oncology Clinic, please call Jeannine Clutter at 504-842-7721.
For 24/7 phone consults and/or patient transfers, please call the Regional Referral Center at 1-855-OHS-LINK (647-5465).