

KIDNEY CANCER UPDATE

Brought to you in conjunction with the Kidney Cancer Association

Starting with this issue, *Clinical Advances in Hematology & Oncology* is launching a bimonthly column on kidney cancer in conjunction with the Kidney Cancer Association. The column will include information about the state of research, advances in treatment, and other news for oncologists who treat patients with kidney cancer. We will begin with an overview of the Kidney Cancer Association and its mission.

An Overview of the Kidney Cancer Association

The Kidney Cancer Association (KCA) is a charitable organization made up of patients, family members, physicians, researchers, and other health professionals globally. It is the world's first international charity dedicated specifically to the eradication of death and suffering from renal cancers. It is also the largest organization of its kind, with members in more than 100 countries.

KCA funds, promotes, and collaborates with the National Cancer Institute (NCI), the American Society for Clinical Oncology (ASCO), the American Urological Association (AUA), and other institutions on research projects. It educates families and physicians, and serves as an advocate on behalf of patients at the state and federal levels in the United States and globally.

KCA was founded in 1990 by a small group of patients, including Eugene P. Schonfeld, PhD, and medical doctors in Chicago, Illinois. In its nearly 25 years as an organization, KCA has made substantial progress in assisting patients and families and raising the visibility of renal cancers.

Among its key activities are:

Research. KCA has placed a strong focus on promoting research in kidney cancer. The organization supports researchers in academic medical centers, government, and industry with money and information, and serves as a catalyst for new ideas. For example, KCA provides financial grants for basic research into the biology of kidney cancer.

KCA's partnership with EmergingMed has resulted in the referral of patients to sites conducting clinical trials. It has also made grants to the AUA Foundation and to the Conquer Cancer Foundation of ASCO to support the work of young investigators (see the examples on the opposite page), and supports other research organizations as well.

Education. During a typical year, KCA provides more than 50 education and support opportunities for patients, survivors, and caregivers in various US cities, including national meetings featuring kidney cancer experts. Supplemental educational materials are distributed at many of these meetings.

The KCA hosts online informal Facebook Group interactions for survivors and caregivers, and its Facebook presence has grown to include more than 85,000 people around the globe. KCA recently launched KidneyCancer.me, a peer-to-peer collaboration website for patients, survivors, and caregivers.

KCA's Nurse Advisory Board has created a book, *We Have Kidney Cancer*, which has helped promote the importance of kidney cancer as a health issue in the United States. To date, *We Have Kidney Cancer* has been translated into 13 languages and is distributed all over the world. KCA strives to offer a new translation each year. Its website, kidneycancer.org, is the international leader in providing kidney cancer information for both the public and for those engaged in clinical medical practice. Its Nurse Hotline answers hundreds of calls from patients each year with questions about their care.

KCA sponsors kidney cancer symposiums both domestically and abroad, and distributes information to thousands of patients, health professionals, and other stakeholders via monthly e-newsletters and *Kidney Cancer News*, a monthly video magazine.

Advocacy. KCA serves as the voice of the kidney cancer community, representing the needs of patients, families, and health professionals. In its role as an advocate on behalf of patients, it collaborates with organizations such as the Cancer Leadership Council, the Foundation for the National Institutes of Health (NIH), the National Cancer Comprehensive Network, the Patient Advocate Foundation, the National Coalition for Cancer Research, Friends of Cancer Research, and various groups concerned with improving the nation's health care.

KCA is also working actively with institutions interested in conducting cancer research, including participation on various committees of the NIH. As a global advocate, KCA participates in meetings all over the world aimed at increasing public awareness of the need for improvement of public health care and the promotion of research.

For more information about KCA activities, visit www.kidneycancer.org.

Focus on Research Funded By KCA

Predicting Response to mTOR Inhibitors

Dr Martin Voss of the Memorial Sloan Kettering Cancer Center in New York, New York, undertook research in patients with advanced renal cell carcinoma. He and his fellow researchers wanted to know why certain patients taking mammalian target of rapamycin (mTOR) inhibitors experience an unusually long benefit from treatment, whereas others have minimal benefit or no benefit at all.

To find out, the researchers reviewed the medical records of approximately 300 patients at Memorial Sloan Kettering treated with temsirolimus (Torisel, Wyeth) or everolimus (Afinitor, Novartis) for kidney cancer. They identified 6 patients with an especially long benefit, and 4 patients with a complete lack of anticancer effect. Whole-exome sequencing was used to analyze the protein-coding regions in DNA of tumor tissue taken from these individuals. In addition, a separate sequencing method that allowed for deeper analysis of subtle changes in the genetic code was used to examine 230 cancer genes.

An analysis of 5 of the 6 long-term responders was published online in *Clinical Cancer Research* in March 2014. The researchers found that tumors from 3 of the 5 patients exhibited mutations leading to functional loss of TSC1, and that 1 of these patients also had a mutation leading to functional gain of mTOR. The researchers also found that genetic changes varied among different tumor sites in the same individual.

This work, which was funded through the Conquer Cancer Foundation, is an important step toward predicting which patients are most likely to respond to mTOR inhibitors.

Variations in Surgical Treatment of Early-Stage Kidney Cancer

Dr David C. Miller, who is now an assistant professor at the University of Michigan, used his award—which was granted through the AUA—to study various approaches to surgical treatment of patients with early-stage kidney cancer.

When partial nephrectomy and minimally invasive nephrectomy emerged as alternatives to open radical nephrectomy, Dr Miller and his colleagues wanted to find out how these newer procedures might benefit patients, and which patients were more likely to receive them.

To examine this, the researchers used linked Surveillance, Epidemiology, and End Results-Medicare data. In one study, they identified 10,866 patients who had undergone partial or radical nephrectomy between 1991 and 2002. They found that in the years spanning 2000 to 2002, the risk of adverse renal outcomes was significantly lower for those undergoing

partial nephrectomy (16.4%) than those undergoing radical nephrectomy (21.8%). There was no difference seen in adverse cardiovascular outcomes. These results were published in *Cancer* in February 2008.

In a separate study, the researchers identified 5483 patients who had been treated with surgery for kidney cancer between 1997 and 2002. They found that 611 patients had undergone partial nephrectomy and 4872 had undergone radical nephrectomy; the procedures were performed laparoscopically in 43 and 515 patients, respectively. After adjusting for patient demographics, comorbidity, tumor size, and surgeon volume, the variance attributable to surgeon factors was 18.1% for partial nephrectomy and 37.4% for laparoscopy. Both of these percentages were higher than the percent of total variance attributable to patient characteristics. These results also were published in *Cancer* in April 2008.

Dr Miller has gone on to publish numerous additional studies, and received a Urology Care Foundation/Astellas Rising Star in Urology Research Award from 2011 to 2014.

Resistance to Selective RAF Kinase Inhibitors

Dr Eliezer Van Allen of Dana-Farber Cancer Institute in Boston, Massachusetts, studied patients with *BRAF* V600-mutant melanoma in order to learn more about why most patients develop resistance to selective RAF kinase inhibitors.

Dr Van Allen and his coinvestigators looked at tumors from 45 patients with *BRAF* V600-mutant metastatic melanoma who had received treatment with either vemurafenib (Zelboraf, Genentech/Daiichi Sankyo) or dabrafenib (Tafinlar, GlaxoSmithKline). Using whole-exome sequencing on formalin-fixed, paraffin-embedded tumors, they found genetic alterations in known or putative RAF inhibitor resistance genes in samples from more than half the patients (51%). Mutations that previously had been found to confer resistance to RAF inhibitors included *NRAS*, *BRAF*, and *MEK1*. In addition, the researchers found that mutations in *MEK2*, *MITF*, were associated with resistance. Mutations in *HOXD8*, and *RAC1*, along with alterations in the phosphoinositide 3-kinase (PI3K) pathway, were unclearly associated with resistance.

The researchers, whose study was published in *Cancer Discovery* in January 2014, stated that learning more about a tumor's specific resistance characteristics could help doctors in their choice of drug, and help researchers identify agents to develop.

Dr Van Allen received a Young Investigator Award from the Conquer Cancer Foundation of ASCO that was supported by the Kidney Cancer Association.