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.

**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.
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 antitumor 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; 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.