UCLA KIDNEY CANCER PROGRAM:

Targeted Drugs Revolutionizing Treatment

Dramatic strides are being made in the treatment of metastatic kidney cancer as UCLA Kidney Cancer Program and other researchers develop targeted therapies – drugs that, unlike the more toxic chemotherapy, aim specifically at killing cancer cells without harming normal cells.

These new drugs have been facilitated by the great progress that has been achieved over the last decade by kidney cancer scientists – led by those at UCLA – in understanding the molecular mechanisms involved in the disease, which has, in turn, made kidney cancer a popular subject of pharmaceutical research. "Now that we have a better idea of the chain of events that are occurring in kidney cancer, we can use drugs that break one of the links in the chain," says Dr Arie Belldegrun, surgical director of the UCLA Kidney Cancer Program. "That's what is happening now, and it's translating to improved survival for patients."

In late 2005 and early 2006, two targeted drugs were approved by the U.S. Food and Drug Administration for treating advanced kidney cancer: Sutent and Nexavar. A third, CCI-779, has shown great promise in clinical trials at UCLA, and a fourth, Avastin, which is approved for treating colorectal and lung cancers, is also being tested in kidney cancer. All of these drugs target biological and molecular mechanisms that researchers at UCLA and elsewhere have found to be involved in the growth and progression of kidney cancer, including proteins such as Vascular Endothelial Growth Factor (VEGF), Platelet Derived Growth Factor (PDGF) and Tumor Growth Factor Alpha (TGF-α).

Sutent and Nexavar were the first two drugs to be approved for the treatment of kidney cancer since 1992, when the FDA approved Interleukin-2 based on pioneering research by Dr Belldegrun and colleagues at UCLA showing that it was effective, in combination with surgery, in treating some kidney cancer patients. In the ensuing years, considerable progress was made in treating metastatic kidney cancer thanks largely to strategies to stimulate the immune response to tumor antigens. So-called immunotherapy using Interferon alpha (Inf-α) and Interleukin-2 (IL-2) is expected to continue to play an important role in kidney cancer treatment, perhaps in combination with emerging targeted therapies – a strategy that is among those currently being tested in UCLA Kidney Cancer Program clinical trials.

The UCLA program was also at the forefront in the clinical trials that led to the approval of Sutent, which has become first-line therapy for metastatic kidney cancer patients. The first patients put on Sutent were at UCLA, and a large study that was instrumental in the drug's approval involved UCLA patients. Dr Fairooz Kabbinavar, the UCLA Kidney Cancer Program's medical director, has played an instrumental role in the development of Avastin and other anti-VEGF drugs, which block the tumor's blood supply.

"The previous drugs we were using to treat metastatic kidney cancer were fairly toxic, and only a handful of patients responded to those treatments," says Dr Kabbinavar. "These new targeted drugs are taken orally, have much more manageable side effects, and have shown significant benefit in many patients. This has provided us with additional, potentially effective treatment options."

With the emerging FDA-approved and experimental targeted therapies – which are typically given in combination with surgery – the UCLA Kidney Cancer Program is better able to designate metastatic patients for drug treatments based on the molecular profile of their tumor and how, as a result of that profile, they are expected to respond to a given approach. Taking advantage of its vast database of patients treated over a 15-year period, the program has developed measures for determining patients' prognosis and deciding who requires the most aggressive therapy (see the accompanying article on page 9). "Kidney cancer is actually multiple diseases that we need to treat differently," explains Dr Kabbinavar. "Using various combinations of these new drugs with surgery and chemotherapy, we are moving toward an era of personalized kidney cancer therapy."