

WEB EXCLUSIVES

Kidney Cancer Expert Shares Insight on New Therapies

BY MELISSA WEBER

The story of treating kidney cancer recently underwent a few revisions, shifting from a tragic tale to one of improved survival. A new understanding of the cancer's biology and therapies to address those intricacies led Robert Figlin, MD, to tell a group of his peers, "The expected survival of a patient with metastatic kidney cancer [in] 2009 is approaching three years. For those of us who have been here, it's quite a difference from the days of the 1970s and 1980s when we basically just watched as these people died."

Figlin, director of the kidney cancer program at City of Hope Comprehensive Cancer Center in Duarte, California, updated a group of nearly 200 physicians, nurses, and other health care professionals about the latest developments in kidney cancer at the Practical Applications of New Agents in Oncology conference in early March in San Antonio, Texas.

In addition to Sutent (sunitinib), Nexavar (sorafenib), and Torisel (temsirolimus)—all approved by the Food and Drug Administration within the past few years—Figlin told the crowd he expected an mTOR inhibitor called everolimus and the antiangiogenic drug Avastin (bevacizumab) to be approved this year for kidney cancer. Indeed, three weeks later, everolimus was approved under the trade name Afinitor for advanced kidney cancer patients whose cancers progressed on Sutent or Nexavar.

Other agents he foresees as FDA-approved within the next two years are axitinib and pazopanib, both of which inhibit angiogenesis (the growth of blood vessels to the tumor). As the basket of new drugs fills, doctors are finding that when patients' tumors stop responding to one drug, they can prescribe another targeted drug and extend survival.

Although it might seem that combining two targeted agents would be better than one, in kidney cancer, that has yet to prove true. Instead, Figlin said using these agents in sequence has produced "incredible survival advantages for patients," while the combinations have been "fraught with potential additive and synergistic toxicity."

While his presentation focused on the newest drugs for kidney cancer, an audience member queried Figlin about his use of immunotherapy drugs, such as interleukin-2 (IL-2) and interferon, which have long been a standard of care.

"The era of immunotherapies is certainly not gone," Figlin responded. "You cannot walk away from the fact that 5 to 8 percent of patients can be cured

forever from a drug called IL-2.”

Although researchers still don't know what it is about those patients that causes such a dramatic response to IL-2, Figlin and his colleagues at City of Hope recently discovered something new about Sutent's effect on the immune system. Beyond inhibiting the vascular endothelial growth factor receptor involved in angiogenesis, new research indicates that Sutent blocks a protein called STAT3 (signal transducer and activator of transcription 3) that, when activated, helps cancer cells evade an assault by the body's immune system.

The research, published in the March 15 issue of the journal *Cancer Research*, found that by inhibiting STAT3, Sutent essentially sets the cancer up for an immune attack—a finding that could lead to the development of STAT3 inhibitors.

To capitalize on the immune effects of Sutent, Figlin noted that he and his team are about to start a trial of Sutent followed by a therapy directed at T cells, a type of immune cell that can kill cancer cells under certain conditions.

Figlin advised the group of cancer professionals that “even though they're [touted as] VEGF-targeted agents, we still don't have a clear understanding of those other targets that they hit, so be open to the possibility that there's more to learn here.” This may be true of many drugs whose complex mechanisms of activity are not always what they seem to be, pointing to the importance of fully understanding the biology behind drugs even after they are approved.

The meeting was hosted by the University of Texas Health Science Center at San Antonio's Cancer Therapy and Research Center, well known for its San Antonio Breast Cancer Symposium held each December. Read more about kidney cancer treatment in the upcoming Summer issue of *CURE*, available this June.